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MARCH, 1956

NO. 3

AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY

Editors

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WILLIAM J. DIECKMANN

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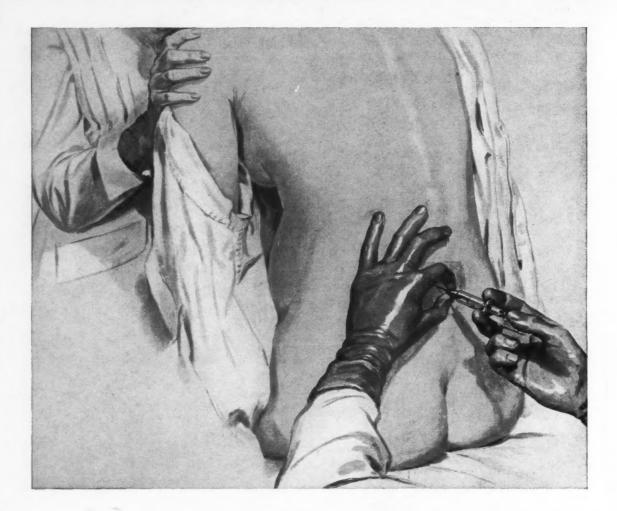
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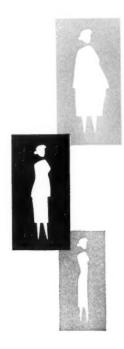
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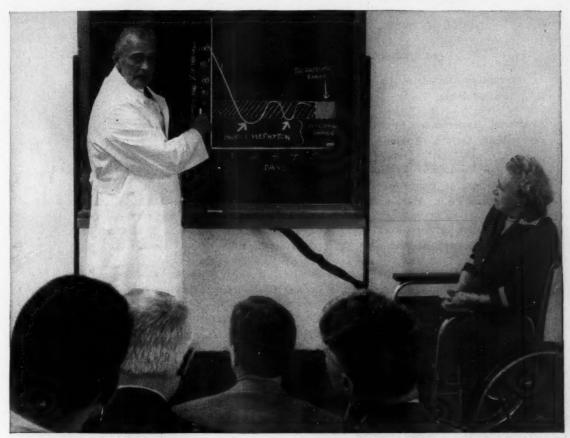
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*Verse by RICHARD ARMOUR Illustrations by LEO HERSHFIELD

IGNORANCE ISN'T BLISS*

There is an awful, quite unlawful,

Violent and dread ache

That should have fame and Latin name

And yet is called "a headache."

The victim thinks his head's in kinks,
Or, from the inner clamor,
Some hidden sprite with all his might
Is banging with a hammer.

He seems to feel that rods of steel

Are thrusting through his cranium.

In state so vile, he couldn't smile

To hear he'd struck uranium.

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References: 1. Illinois M. J. 105:305 (June) 1954. 2. Obstet. & Gynec. 1:94 (Jan.) 1953. 3. Bull. Margaret Hague Maternity Hosp. 6:107 (Dec.) 1953. 4. Missouri Med. 51:727 (Sept.) 1954. 5. J. Michigan State M. Soc. 53:862 (Aug.) 1954.

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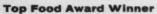
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¹Whyte, D. W., "Special Indications for Rectal Pentothal in Children", Canad. Med. J., 64:525, June, 1951

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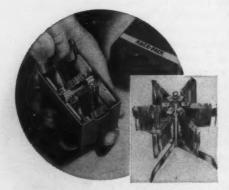


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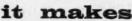
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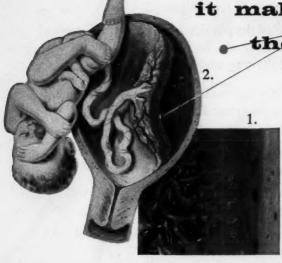


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REFERENCES

- Dill, L. V., Med. Annals of D. C. 23:12, 1954
 Greenblatt, R. B., Obst. & Gyn. 2:5, 1953
 Javert, C. T., Obst. & Gyn. 3:4, 1954



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- Crunden, A. B., Jr., and Davis, W. A.: Am. J. Obst. & Gynec. 65:311, 1953.
- 2. Bradley, J. E., et al.: J. Pediat. 38:41, 1951.
- 3. Tebrock, H. E., and Fisher, M. M.: M. Times 82:271, 1954.



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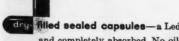


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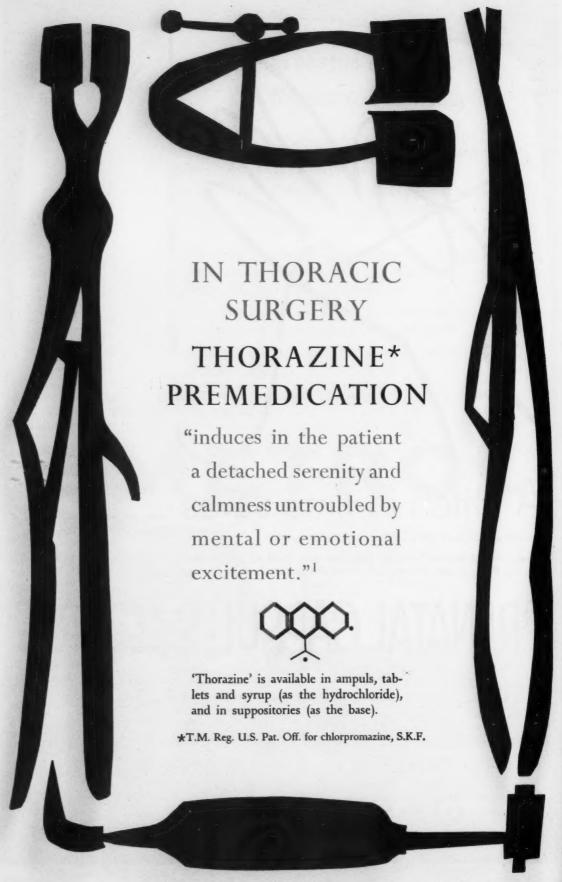
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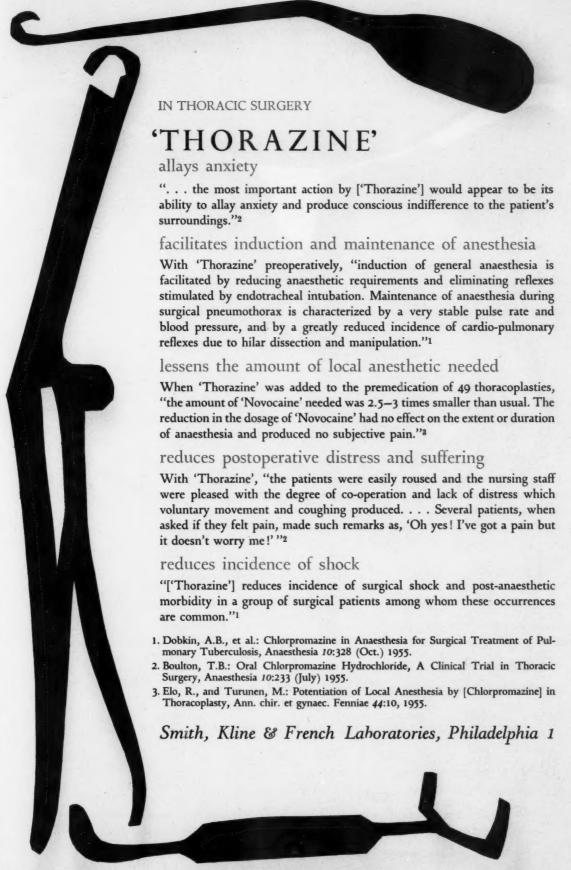


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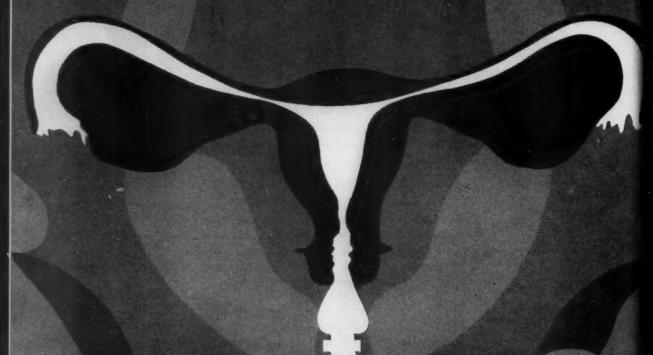


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he available evidence indicates that one of every four or five adult women harbor the parasite . . . there are many recorded data suggesting coitus as a method of transfer."

T.v. conquers man. "In the present study (926 men) there is a total of 144 cases harboring Trichomonas vaginalis.... This is a percentage incidence of 15.5.... The percentage incidence of non-specific urethritis cases which may be attributable to Trichomonas vaginalis was 36.9 percent." Karnaky found the infection in the urethra and prostate and under the prepuce of 38 among 150 husbands with infected wives.

Few symptoms—little concern. "The [female] patient seeks medical attention because of . . . leukorrhea . . . intense itching, dyspareunia and burning and frequency of urination." However, when the male patient has an infection, he often considers the signs and symptoms as insignificant and accepts them with little or no concern. 5

Protect the wife. In preventing re-infection, Trussell states, "Obviously a condom will be the most effective mechanical barrier. Eradication of the parasite in both sexual partners is of course the ideal." Karnaky recommends that the husband wear a condom for four to nine months whenever Trichomonas vaginalis is resistant and recurrent.

IN VAGINAL TRICHOMONIASIS

Prescribe top-grade condoms. To eliminate trichomonads "once and for all," take specific measures to win co-operation of the husband. In prescribing a condom, be selective and take advantage of Schmid product improvements.

When there is anxiety that the condom might dull sensation, the answer is to prescribe XXXX (FOUREX)[®] skins. Made from the cecum of the lamb, they feel like the patient's own skin, are pre-moistened and do not retard sensory effect. If cost is a consideration, prescribe RAMSES,[®] a transparent, tissue-thin, yet strong condom of natural gum rubber. SHEIK,[®] also a natural gum rubber condom, is even more reasonable in price.

Any husband, any wife, in your practice, would prefer to hand the druggist your prescription for a condom, rather than to ask for it "in public." Isn't that true? This is another instance of diplomacy in medicine to prevent an embarrassing situation. To assure finest possible quality and earn appreciation for your thoughtfulness, prescribe XXXX (FOUREX), RAMSES or SHEIK condoms by name. Prescribe Schmid protection for as long as four to nine months after the wife's infestation has cleared. The protection Schmid condoms afford is the very foundation of re-infection control.

References:

1. Trussell, R. E.: Trichomonas Vaginalis and Trichomoniasis, Charles C. Thomas, 1947, Springfield, Illinois. 2. Feo, L. G. Am. J. Trop. Med. 24:195 (May) 1944. 3. Karnaky, K. J.: Urol. and Cutan. Rev. 42:812 (Nov.) 1938. 4. Kanter, A. E.: Postgrad. Med. 12:457 (Nov.) 1952. 5. Glen, J. E., Jr., and Bailey, R. S.: J. Urol, 66:294 (Aug.) 1951. 6. Karnaky, K. J.: J.A.M.A. 155:876 (June 26) 1954.

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Superior to vinegar and simple acid douches

In recommending a vaginal douche, your patients will appreciate your consideration of feminine daintiness. The clean refreshing fragrance of Massengill Powder makes it most acceptable for feminine hygiene.

Unlike simple acid douches, Massengill Powder is buffered to maintain the required acid pH of the vagina. And its low surface tension permits it to penetrate into and cleanse the folds of the vaginal mucosa.

Indications

Massengill Powder solutions are a valuable adjunct in the management of monilia, trichomonas, staphylococcus and streptococcus infections of the vaginal tract.

Routine douching with Massengill Powder solutions minimizes subjective discomfort and maintains a state of cleanliness and normal acidity without interfering with specific treatment.

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The buffered acid vaginal douche

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"the gratitude of the patient is ample reward"...

"Vaginal discharge is a common complaint amongst
women of all ages ... this is one of the conditions
in which the gratitude of the patient is ample
reward for the time and trouble spent in treatment,"
states one investigator. Gantrisin Vaginal
Cream is highly effective against

many sulfonamide-susceptible

microorganisms which are

frequently found in vaginal and

cervical infections. Its acid

pH of 4.6 promotes the return

of the flora found in a

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Page 26

ideal endocrine "companion" for menopausal patients



comforts—Controls major symptoms within 6 to 10 days, hot flushes in as few as 3 days.

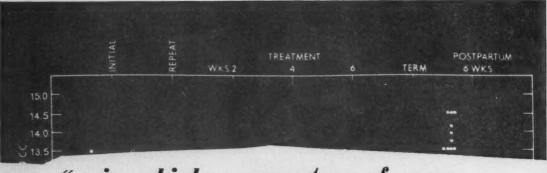
cheers—Confers a welcome feeling of physical vitality and mental well-being.

compatible—Much less prone to cause the side effects so often experienced with stilbene derivatives.

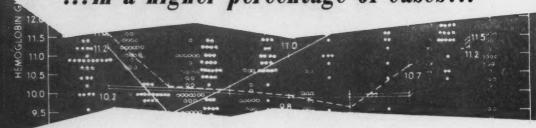
thrifty - Does "a better job at far less cost" and is "much better to use than any of the so-called naturally conjugated estrogens."*

*Clinton, M., Round Table Discussion: New York J. Med. 56:481, 1954. Estinyt, © brand of Ethinyl Estradiol U.S.R.

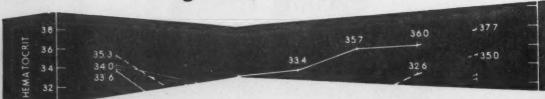
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"... in a higher percentage of cases...



... a greater increase



in hemoglobin concentration...



... with almost no side reactions."*



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Forman, J. B.: Anemia of Pregnancy, Connecticut M. J. 14: 930 (Oct.) 1950. Extensive bibliography on request.

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The CLASSICAL Vaginal Therapeutic



An amazing abundance of "new" concepts in treatment are on continuous parade for one of the most vexing of all problems, the patient with the trouble-some vagina. Consider the rationale of one product, AVC Improved, accepted, and in ever-expanding use these 12 years, which contains the best of these "new" ideas that have long been recognized by the medical profession.

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Containing only the active principle of the thyroid gland, SYNTHROID Tablets are odorless, tasteless and free from all impurities. Activity is measured by weight and not by biological standardization. All batches are absolutely identical so that dose-for-dose uniform clinical effect is assured.

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"Trilene," self administered with the "Duke" University Inhaler, under proper medical supervision, provides highly effective analgesia with a relatively wide margin of safety.

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The "Duke" University Inhaler (Model-M) is specially designed for economy, facility of handling, and ready control of vapor concentration.

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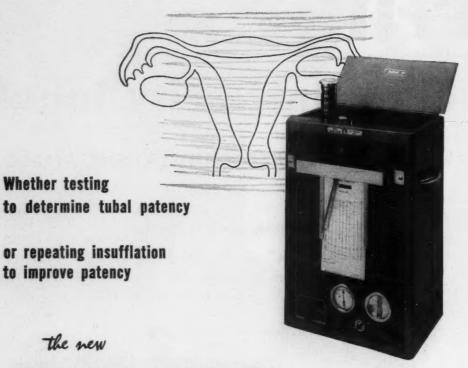
- Induction of analgesia is usually smooth and rapid with minimum or no loss of consciousness
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"Trilene" alone is recommended only for analgesia, not for anesthesia nor for the induction of anesthesia. Epinephrine is contraindicated when "Trilene" is administered.

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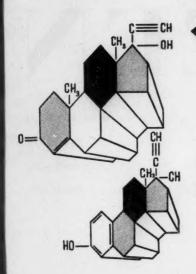
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Habitual abortion, threatened abortion, functional sterility, dysmenorrhea, and premenstrual tension have responded to DUOSTERONE therapy.

DUOSTERONE simulates the normal ovarian endocrine pattern of the secretory phase of the menstrual cycle. A normal cycle may be set off by DUOSTERONE stimulation, much as touching the pendulum starts a wound clock. Normal menstrual function is safely and conveniently restored with essential, two-hormone action provided by DUOSTERONE: (1) Administration of needed progesterone, and (2) Estrogen priming, which is indispensable to adequate progesterone activity.

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action

5 to 10 tablets per day for five days, beginning exactly one week before expected onset of menses. No medication is given on last two days. Repeat dosage for six successive cycles to ensure reestablishment of normal function.

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Bottles of 25 and 100 tablets. On prescription only.

*Am. J. Obst. & Gynec., 68:1321, 1954.

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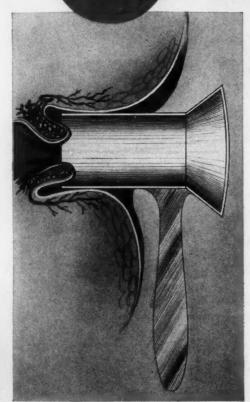
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Greater comfort in hemorrhoidal and simple inflammatory rectal conditions is now possible with PNS Suppositories—a combination of anesthetic, decongestive and bactericidal ingredients.

FORMULA: Each suppository contains the following in a cacao butter base:

Pontocaine® hydrochloride 10 mg. Neo-Synephrine® hydrochloride 5 mg. Sulfamylon® hydrochloride 0.2 Gm. Bismuth subgallate 0.1 Gm. Balsom of Peru. 50 mg.

With PNS Suppositories pain is quickly brought under control; swelling and inflammation are reduced; infection is combated. Indicated for the relief and symptomatic treatment of uncomplicated hemorrhoids; before and after hemorrhoidectomy or sclerosing therapy.

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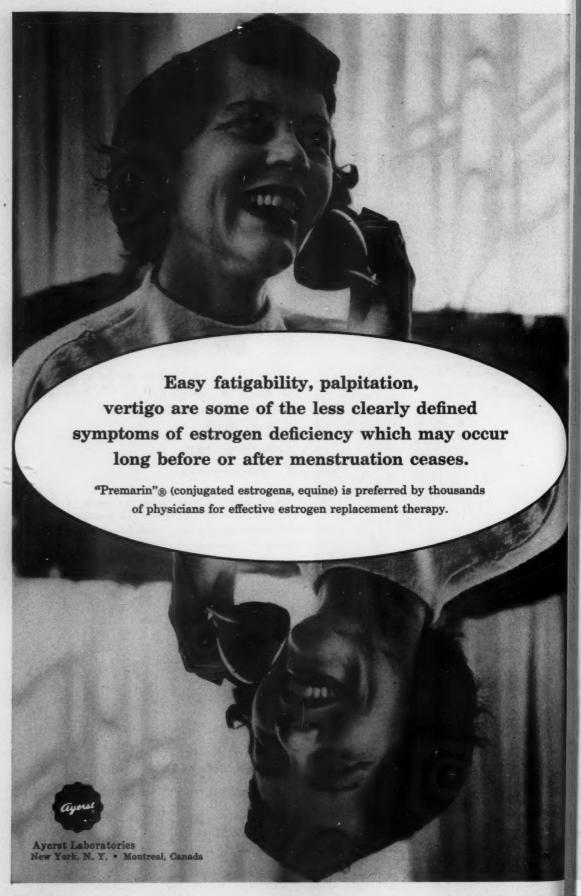
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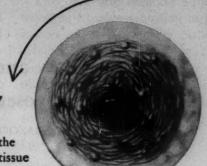
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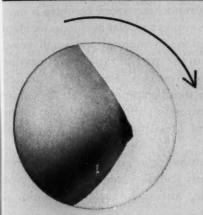




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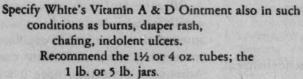


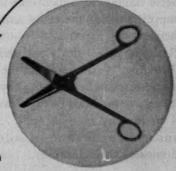
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A Laboratory and Clinical Report on Adrenosem® Salicylate

(BRAND OF CARBAZOCHROME SALICYLATE)

History

The first investigation of a hemostat with an action comparable to Adrenosem Salicylate was made by Derouaux and Roskam¹ in 1937. They reported that an oxidation product of adrenalin, adrenochrome (which has no sympathomimetic properties), has prompt hemostatic activity.

It was further found that various combinations of adrenochrome, notably the oxime and semicarbazone, produced stable solutions. But, these were so slightly soluble that sufficient concentration could not be obtained for practical therapeutic use. By combining these adrenochrome compounds in a sodium salicylate complex a stable, soluble form can be obtained. This complex has been given the generic name, carbazochrome salicylate, and is supplied under the trade name Adrenosem Salicylate.

Roskam, in his study entitled "The Arrest of Bleeding,"2 enumerates "the drugs whose efficaciousness as hemostatics have been proved by accurate methods in experimental animals and in healthy men as well.... One is the monosemicarbazone of adrenochrome [Adrenosem Salicylate]."

Chemistry

Adrenosem Salicylate is a synthetic chemical. The full chemical name is adrenochrome monosemicarbazone sodium salicylate complex.

Pharmacology

Although it is chemically related to epinephrine, Adrenosem Salicylate has no sympathomimetic effects. It does not alter blood components, nor does it affect blood pressure or cardiac rate.2-7

Sherber, in an early study,3 concludes that Adrenosem Salicylate * "is a potent antihemorrhagic factor in those conditions in which the integrity of the smaller vessels is interrupted. and is superior to any similar material that is now available."

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He continues, "From our experience it appears that adrenochromazone complex is indicated in preventing vascular accidents inciden to hypertension; in maintaining small vesse integrity; in the preoperative preparation where oozing from a vascular bed is anticipated, as in tonsillectomies, adenoidectomic and prostatectomies; and as an adjunct in the treatment of bleeding from such surgical procedures."

Adrenosem Salicylate may be administered simultaneously (but separately) with any type of anesthetic, anticoagulant, or vitamin I and heparin.

A Unique Systemic Hemostat

Clinical investigators²⁻⁷ are in agreement that Adrenosem Salicylate controls bleeding and oozing by decreasing capillary permeabilit and by promoting the retraction of severe capillary ends. It aids in maintaining norm capillary integrity by direct action on the intercellular "cement" in capillary walls. The interesting work of Fulton⁸ confirms this Adrenosem Salicylate, since it is not a vas constrictor, has no effect on large severe blood vessels and arterioles.

Adrenosem Salicylate is being used bot prophylactically and therapeutically in thou sands of hospitals, and in virtually every typ of surgical procedure. It has also proved mo useful in dental surgery.7

Owings reported on the use of Adrenose Salicylate in controlling postoperative adend bleeding in 102 cases.4 "We have used 21/2 m NEW (½ ampule) intramuscularly, 15 minutes before anesthesia for children and 5 mg. (1 ampule) for adults." In only one patient did bleeding occur. Three others showed red blood from the nose and mouth. These patients "were then given 5 mg. intramuscularly, with prompt and complete control. We have also noticed that bleeding stopped more promptly on the operating table."

This is a 1% incidence of postoperative bleeding using Adrenosem Salicylate preoperatively, compared to an incidence of 10% postoperative bleeding in all cases taken from previous records, without Adrenosem Salicylate medication.

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Peele reports on the use of Adrenosem Salicylate in treating 178 patients with 24 different conditions. The drug was first used to control postoperative hemorrhage from the adenoid region. He adds: "The results were so dramatic that since that date [1953] Adrenosem Salicylate has been used postoperatively to reduce bleeding from all otolaryngologic and bronchoesophagolic procedures, to treat postoperative hemorrhage from the tonsil and adenoid regions, and to treat selected cases of epistaxis."

The effectiveness of Adrenosem Salicylate in controlling bleeding and oozing in 330 patients is reviewed by Bacala.6 "Our experience of the effect of carbazochrome salicylate on 317 surgical indications and 13 obstetricogynecological conditions, has been therapeutically encouraging and successful for the control of capillary bleeding. Foremost among the cases studied were 223 tonsillectomies definitely benefited by this metabolic hemostat, making a diminution of the control incidence of posttonsillectomy bleeding of 19.8% down to 7%. It has also been found useful in gastro-intestinal bleeding, cataract extraction, epistaxis, incisional seepage, trans-urethral prostatectomy, menometrorrhagias, cervical ooze, antepartum and postpartum bleeding, threatened abortion, and prevention of capillary hemorrhages during hedulin or dicumerol therapy."

Side Effects

All investigators concur that, at recommended dosage levels, Adrenosem Salicylate is free from toxic effects. No cumulative effects attributable to the drug have been reported.

The only side reaction noted has been a transient stinging sensation in the area of injection when Adrenosem Salicylate is used intramuscularly. As one investigator comments: "The brief discomfort which attends the injection of Adrenosem into the gluteal region has not been a significant problem in children or adults as originally anticipated." 5

Indications

Idiopathic purpura, retinal hemorrhage, familial telangiectasia, epistaxis, hemoptysis, hematuria.

Postoperative bleeding associated with: tonsillectomy, adenoidectomy and nasopharynx surgery; prostatic and bladder surgery; uterine bleeding; postpartum hemorrhage; dental surgery; chest surgery and chronic pulmonary bleeding.

Dosage

For recommended dosage schedules, please send for detailed literature.

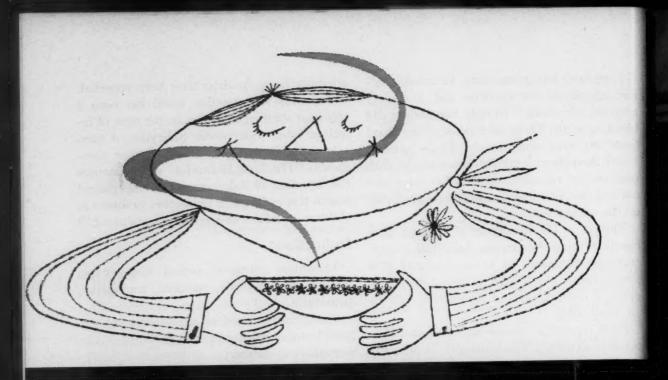
Supplied

Ampuls: 5 mg., 1 cc. (package of 5).
Tablets: 1 mg. S.C. Orange, bottles of 50.
Tablets: 2.5 mg. S.C. Yellow, bottles of 50.
Syrup: 2.5 mg. per 5 cc. (1 tsp.), 4 ounce bottles.

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AVAILABLE AT ALL PHARMACIES in convenient packages of 24 individual 3 Gm each containing 35% Alkyl Aryl sulfonate (surface active and detergent), .33% ethylene bis-iminodiacetate (chelating agent), 53% Sodium sulphate, 2% Ox sulfate and 9.67% dispersant.

Full treatment package and literature on request.



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confirms and defines superiority over other Rauwolfia preparations in the treatment of HYPERTENSION

- Rauwiloid represents the balanced, mutually potentiated actions¹ of several Rauwolfia alkaloids, of which reserpine and the equally antihypertensive rescinnamine have been isolated.
- Hence, reserpine is not the total active antihypertensive principle of the rauwolfia plant.
- Rauwiloid is freed of the undesirable alkaloids of the whole rauwolfia root. Recent investigations confirm the desirability of Rauwiloid (because of the balanced action of its contained alkaloids) over single alkaloidal preparations; "...mental depression...was...less frequent with alseroxylon..."2

The dose-response curve of Rauwiloid is flat, and its dosage is uncomplicated and easy to prescribe...merely two 2 mg. tablets at bedtime.

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Cronheim, G., and Toekes, I. M.; Comparison of Sedative Properties of Single Alkaloids of Rauwolfia and Their Mixtures, Meet, Am. Soc. Pharmacol. & Exper. Therap., Iowa City, Iowa, Sept. 5, 1955.

^{2.} Moyer, J. H.; Dennis, E., and Ford, R.: Drug Therapy (Rauwolfia) of Hypertension. II. A Comparative Study of Different Extracts of Rauwolfia When Each Is Used Alone (Orally) for Therapy of Ambulatory Patients with Hypertension, A.M.A. Arch. Int. Med. 96:530 (Oct.) 1955.



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- REFERENCES

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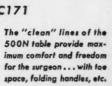
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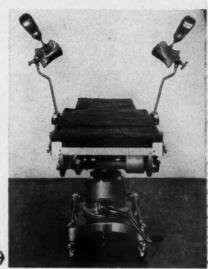
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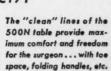
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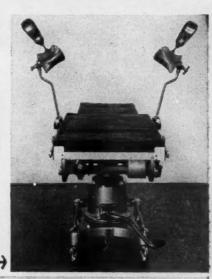
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A brief chapter on normal labor and another concerning the normal puerperium as a basis for the discussion of the management of complicated delivery and of postpartum disorders have been added. The changes which occur in the maternal organism in response to pregnancy are not consolidated in a separate section but are considered as they relate to and influence each of the complications. In some instances the material was rearranged to permit a single complete discussion of certain conditions rather than to describe their treatment during pregnancy, labor and the puerperium separately; the management of the third stage of labor and the treatment of postpartum hemorrhage, for instance, are considered together, and breech delivery is combined with version and breech extraction which are similar in many respects. The portions of the book on erythroblastosis fetalis and the examination and care of the newborn infant were prepared by Dr. Victor C. Vaughan, III, Assistant Professor of Pediatrics in the Temple University School of Medicine.

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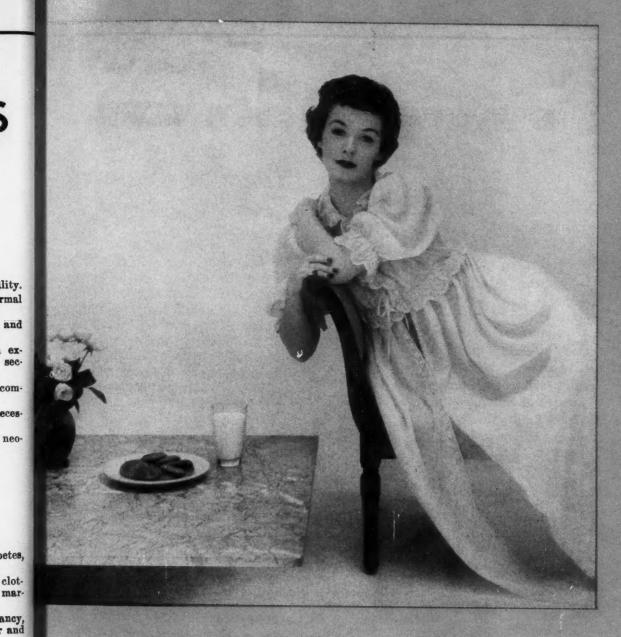
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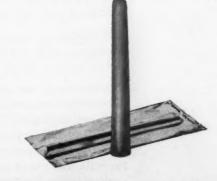
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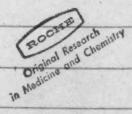
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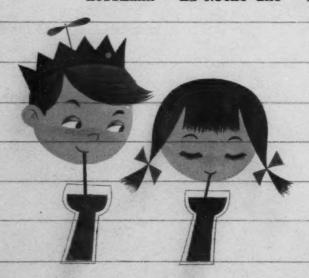
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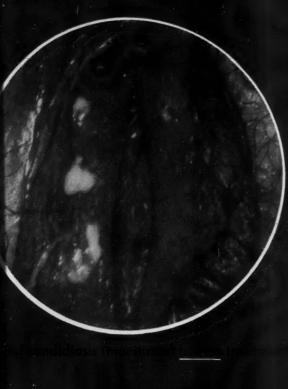
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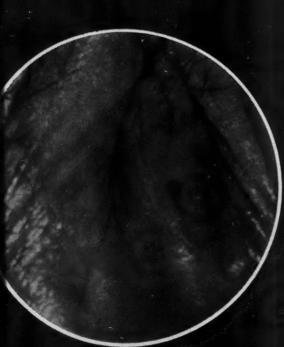
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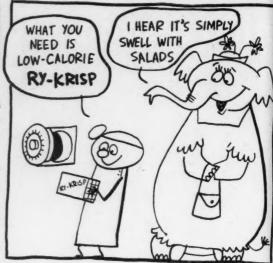
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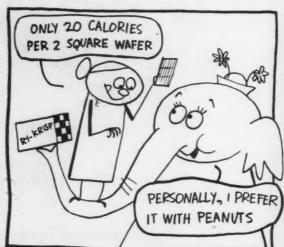
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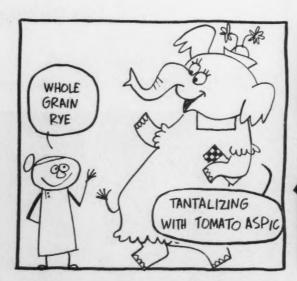














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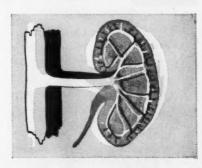
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 Assali, N. S., and Suyemoto, R.: Am. J. Obstet. & Gynec. 64:1021 (Nov.) 1952,

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CONSERVATIVE OBSTETRICS IN A MODERN WORLD*

President's Address

THADDEUS L. MONTGOMERY, M.D., PHILADELPHIA, PA.

E ACH year several thousand presidents of several thousand organizations worriedly prepare several thousand presidential addresses. Universally they fail to realize that their listeners are generally a sympathetic audience, cognizant of their presiding officer's deficiencies, tolerant of his subject material, and ready to be surprised if he presents anything different than the usual run of presidential orations.

Uncomforted by these comforting thoughts, I, like all of your previous presidents, have gone through the process of selecting topics—considering, rejecting, reconsidering, etc. Finally, I concluded that if I were to contribute anything to the archives of this Association which would be worth while I must speak on a subject that is dear to my heart, one that constitutes a lifetime interest, and one that reflects influences and traditions that have been brought to bear throughout my career in medicine.

To many of my close acquaintances, therefore, it will not be a surprise that I have selected a subject which has to do with conservatism in obstetrics, and that my title could be "Conservative Obstetrics in a Modern World."

*Presented at the Sixty-sixth Annual Meeting of the American Association of Obstetricians and Gynecologists, Hot Springs, Va., Sept. 8 to 10, 1955.

Note: The Editors accept no responsibility for the views and statements of authors as published in their "Original Communications."

Perhaps I have also been led to the choice of this topic by recent exposure to a hospital examiner. This gentleman raised his eyebrows at our cesarean rate of something above 6 per cent, and observed that we were not supposed to have over 5. I asked him how many forceps deliveries were permitted. Upon consulting his notebook he stated that the forceps rate didn't seem to make any difference. I suspected that a couple of his superiors in Chicago had gotten to this individual and tipped him off as to what questions to ask in Philadelphia. At any rate I doubt that we received any credit in Paradise for our 8 per cent of forceps deliveries. It appears therefore that one who is officially conservative may do any number of vaginal operations but not more than the prescribed number of abdominal deliveries.

In this situation much depends upon one's definition of conservatism. My Webster dictionary states that "to conserve" means "to keep in a safe or sound state; to save." The definition does not enumerate how many times one does this or that in order to conserve; when the definition is applied to obstetrics a true concept does not seem to depend upon one's precise percentage of forceps, or of cesarean section, or of induction of labor, or of tubal ligation, or upon one's individual prejudices concerning analgesia and anesthesia, breast feeding, rooming-in, etc. The definition points primarily to an attitude of mind, in medicine to a philosophy of practice, a concern for saving tissue, function, and human life. In application, however, conservatism demonstrates itself in a number of ways.

When it comes to defining concisely what is a "modern world," and what part conservatism plays in it, certain difficulties arise. Our earth acquired a hardened, walkable surface some three and a half billion years ago, the oldest fossils are three hundred million years old, mammals made their appearance one and a half million years ago, and man emerged in his present comely form about one hundred thousand years in the past. Changes have been slow, and so-called modern civilization is a flitting moment in the total passage of time.

There is one possibly significant difference, however, between the ancient or prehistoric world, and the modern. Until the appearance of man, animal life was molded in development and ultimate fate by natural surroundings. With the advent of the thinking and calculating mind, homo sapiens adjusted and modified environment to fit his needs and whims; in other words, he began to manipulate the very surroundings which mold his own future.

In this relation and in this manipulation there has been little to smack of the conservative. Man has populated the far corners of the earth with an acquisitive predatory race, he has scratched from the earth's surface its treasures of ore and fuel, he has exhausted stores of food and water, he has destroyed his fellow man with instruments of war and with mechanical contraptions of peace; now he is in a fair way to destroy the very earth upon which he treads.

The appearance upon this scene of a small group of ragged individuals bearing a tattered flag, "Conservative Obstetrics," presents a pitiful, somewhat eomical picture.

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Yet perhaps it is time that a few here or there begin to think about conserving—conserving in general—as well as in obstetrics, about saving things that were at one time considered worth while; minds that are clear to think, families that are a unit of strength, ideals that children may be raised by, homespun virtues which lead the individual to do for others as he would be done by.

Over a period of years the feeling has grown upon me that the obstetrician has more to do with all of this than he has any concept. In his profession he treats with the beginnings of life and the circumstances which surround them, his influence in the home is second only to that of the family doctor with whom he may often be embodied. How he handles the course of pregnancy, the progress in labor, and the procedures of delivery; how he draws together the family around the advent of the newborn may exert more influence upon the future of the race, for good or for evil, than any one other individual may bring to bear.

The effect of what we do today upon the development of the individual tomorrow is difficult to foresee, has never been adequately determined, and is at the moment a matter of conjecture. In the case of gross injury during pregnancy or labor we accept the outcome as significant and unfortunate. Regarding the ultimate effect of more subtle tissue damages we are uncertain. Concerning the emotional factors which surround the function of reproduction and which our psychiatric friends speak of we are prone to scoff.

I suspect that we would all agree, however, that for the two patients concerned in obstetric practice, birth has tremendous significance; to the mother it is the most important event physically and emotionally that she will face in her entire life; to the baby, quite independent of other considerations, it is the most critical physiologic adjustment which the new organism will have to make in its entire existence.

There is unmistakable evidence that, whatever the individual physician may think concerning these subjects, the community at large is beginning to be concerned. Other branches of medicine are asking what relationship obstetrical care has to conditions which arise later. Attention at our obstetric congresses progresses from maternal mortality, to fetal mortality, to fetal morbidity. The Association for the Aid of Crippled Children holds an extended conference on "Prematurity, Congenital Malformation, and Birth Injury." The World Health Organization concerns itself with "Anoxia of the Newborn Infant." The National Institutes of Health consider fetal injuries the number one problem of research in the field of obstetrics.

These problems have a physical and an emotional side. The physical is concerned with the management of pregnancy, the mechanism of labor, the operations of delivery; the emotional with the subtle relationships of parents and baby, and the establishment of the family.

Prenatal care, proper nutrition, avoidance of infection, careful management of toxemia are areas in which great progress and improvement have been made. Hospital surroundings and the facilities of the delivery room, anes-

thesia, the blood bank, and improved surgical techniques have saved many lives. Operative procedures have been devised to meet almost any complicated situation in labor or delivery.

Among such operative procedures, cesarean section has proved to be one of the most merciful and efficacious. Despite its many shortcomings, when the operation is properly applied and performed it constitutes the solution of many of the serious problems of labor. As concern is manifested for fetal interests as well as maternal, the frequency of cesarean section has inevitably and progressively increased.

If the obstetrician subscribes to the philosophy of repeat cesarean section. and if the number of such repeat cesarean sections is not restricted in a given individual to a specific two or three, the cesarean section rate rises in the practice of any one individual or clinic to a considerable height. However, if the operation is thoughtfully selected in the individual case, it is difficult to see how a numerical frequency can be set up as a criterion of obstetric conservatism, or arbitrary limitations defined.

There are other operations which bear a less favorable relationship to conservative practice, among which are internal podalic version and decomposition and extraction of the breech. These procedures, frequently traumatic to the fetus and dangerous to the mother, should be relegated to the past, with the exception of a few individual and rare indications. In most situations where labor is arrested they are better replaced by cesarean section. To apply them to normally progressing labor of the vertex or breech seems inexcusable.

The operation of forceps delivery as now performed stands in a somewhat different category. Performed as a low perineal procedure and as a concluding event in the mechanism of labor the possibilities for ill are lessened. It is difficult, however, to accept the statement of those who routinely use instruments that the fetal morbidity and mortality are less than they would be with spontaneous delivery.

One wonders just what the "prophylactic" forceps prevents. Proponents of low forceps speak of the deleterious "pounding" of the fetal head against the pelvic floor as if it were being beaten down upon that structure by some mighty sledge. If one eliminates from this discussion cephalopelvic disproportion at the outlet, the only "pounding" which the fetal head is subjected to in normal labor is the expulsive pressures from the uterus and abdominal muscles and resistance by the soft parts of the pelvis. As the expulsive forces act, the muscles and soft tissues of the pelvic floor and perineum relax in perfectly synchronous fashion, and with intervening periods of rest.

Unless man devises an episiotomy which reaches up to the spine of the ischium and includes the entire levator ani, as well as the perineal muscles, the pelvic floor must in one fashion or another be dilated before any vaginal delivery can be effected. As for the perineum, it is incised at the moment of birth, in either spontaneous or forceps delivery.

Assuming that the patient is properly attended, the progress of labor carefully followed, and the fetal heart sounds frequently observed, there is nothing in the literature to date which would indicate that the resulting fetal

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mortality of low forceps delivery in normal cases is better than that of spontaneous delivery. The differences that may exist in regard to fetal *morbidity* are a relatively unexplored field.

Actually the best results of which I have heard to date are those at The Preston Retreat, in Philadelphia, where patients are delivered spontaneously by competently trained midwife nurses, episiotomy being performed when necessary. Physician consultation is always available. Episiotomies are repaired in 12 to 24 hours as a separate procedure. Dr. Hirst has promised to report these results before this organization in the near future.

Routine forceps delivery also carries with it a train of routine other procedures which are something less than desirable, namely, deeper anesthesia, rapid delivery by traction, greater trauma of the maternal soft parts, etc. Routine low forceps deliveries have brought with them saddle block anesthesia, and saddle block anesthesia has introduced the problems of a major anesthetic procedure into what otherwise would have been a simple physiologic mechanism.

It seems therefore that the burden rests with the advocates of low forceps to demonstrate that operative delivery is significantly better than spontaneous delivery, rather than for the advocates of physiologic mechanism to prove that spontaneous delivery is safer than low forceps.

In the light of our own experience and upon review of statistics from other clinics I find that if patients with normally progressing labor are permitted to deliver spontaneously, if difficult forceps deliveries are avoided, if a few low perineal forceps are done for instruction purposes, and if forceps are used for mild outlet disproportion and unrotated occiput posteriors, the frequency amounts to somewhere between 6 and 10 per cent. Quite likely as time goes on cesarean section will replace all the more difficult forceps operations; and traumatic delivery, whether by version or forceps, will be an evil memory of the past.

Of the obstetric operations which are accepted in this country as having conserving value, episiotomy properly timed and performed stands preeminent. This simple operation has done much to relieve American women of the distresses in later life of cystocele, rectocele, vesical and fecal incontinence. It must be properly timed, it must not disturb the mechanism of labor, it must not increase the anesthetic risk; otherwise, its dangers exceed its benefits. For these reasons we specify that it be repaired under local anesthesia at the conclusion of the third stage.

Left to herself the average patient reveals a remarkable propensity for spontaneous delivery. Experience with a variety of races and individuals indicates that approximately 85 per cent are subjects for physiologic or normal childbirth. To the observing eye nothing seems too wrong with Nature's mechanism of birth. It is one of the most beautiful physiologic procedures and adjustments in all natural history. Its good features may be nurtured by proper instruction to the mother as to what to expect and how to participate. Carefully controlled analgesia relieves the more painful phases. The continued presence of the accoucheur inspires the confidence and cooperation of the patient.

The satisfaction of accomplishment which is demonstrated by the mother, and the hearty cry of the newborn fetus are ample rewards for the obstetrician who takes the time to see his patient through the course of labor. I suspect that the majority of physicians would prefer their wives and their daughters delivered in some such fashion.

Certain ancillary obstetric operations, such as elective induction of labor and tubal ligation, must be viewed with a critical eye. The reproductive function is too precious a possession to be permanently given up or lightly dispensed with. As for the routine induction of labor, too many reported and too many unreported accidents have occurred to convince the conservative that such procedures approach the efficiency or safety of normally starting labor.

Obstetric practice is a difficult field and arduous work. The temptation to cut corners, to relieve the stress and strain of practice, to appeal to the immediate desires of the patient, to take the easier path, are very great. Unfortunately, when Nature set up her principles of reproduction she did not take into consideration the probability that the birth process would be attended by a busy practitioner. The physiologic mechanisms which were devised prove oftentimes long and distressing. Care of many obstetric patients is difficult for any one individual to cope with. The arrangement of several obstetricians practicing together has done much to make possible the adaptation of the obstetrician's time to the vagaries of practice, instead of trying to adjust delivery to the comings and goings of the physician.

It is a vanity of man to assume that he can beneficially alter the course of normally progressing labor. The processes involved are intricate and far more complex than the most profound physiologic laboratory or experiment that has ever been set up. Thus far in the entire history of the human race no one has been able to improve on, or safely and permanently substitute for, the physiologic mechanisms of the human body, whether they be digestion, assimilation, respiration, elimination, or reproduction.

We would be in much better case today to study these intricate physiologic problems and to concern ourselves with maintaining and nurturing physiology when it exists. Such a practice might also give more time for the study of the many serious complications of pregnancy and labor.

Turning in the final minutes of this paper to the emotional and psychological problems of reproduction one enters a difficult and obscure field. Much has been written but little is known. Authoritative data on these matters will require a lifetime of observation, and even then extraneous factors are likely to influence the results.

In this unsettled area the more important instructors for the moment are common sense, deep-seated feelings of correctness, and observation of the offspring-mother relationship in other forms of mammalian life.

Under natural circumstances the animal mother seeks a secluded and protected area for birth, delivers her young with little aid, nurses the offspring at the breast immediately, protects and nurtures the offspring, lives with and fights to the death for the young. Gradually she brings her litter into contact with the world and teaches them to feed, to obey, to respond to

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the laws of Nature. As the young grow and become more confident the mother gradually nudges them out into the world and finally leaves them to fend for themselves.

Probably there is much that the psychiatrist and the educator, as well as the physician, could learn from this train of events: maintenance of close contact of mother and baby, support of early and sustained breast feeding, warm surroundings and protection of the growing young, teaching of obedience, inducing respect for natural and written law, and ultimate preparation for contacts with the outside world.

These are homely and natural values that are worth thinking about and perhaps reviving.

Summary

This is the close of my remarks. I have said much that is controversial. I have supported policies and philosophies which are unacceptable to many members of this Association. I have shown small sympathy for the individual who thinks that in the case of normal reproduction he has something better to offer than well-governed physiology.

However, in pursuing this subject I have not been addressing the specialists of this group alone. I have been trying to reach out to the small cities and hamlets of this country where practitioners are doing obstetrics and endeavoring to make a safe go of it. From these areas physicians look to our national organizations for support and guidance.

To these physicians seeking to do the best they can with their many problems I wish to direct these final words:

- If you are instructing your patients to approach labor with confidence and courage,
- If you are permitting your normal patients to progress in labor and deliver spontaneously,
- If you consider that birth of a baby is the most important single event of the day and adjust your practice to provide the necessary attention and support to your patient,
- If you employ sedation and anesthesia judiciously,
- If you are alive to the possibilities of complication and are prompt in its correction,
- If you are conservative in the induction of labor and tubal ligation,
- If you encourage mothers to nurse their babies and to participate in baby care,
- If you are thinking not only of the exigencies of the moment but of the effects in the future,
- If you are helping young couples to establish the family and the home,

Then, in the opinion of *this* speaker, you are practicing not archaic or old-fashioned obstetrics but you are giving the finest service that any one person can give to another at the most important time in that other person's life; you are also practicing consistently the type of obstetrics that the profession will inevitably and recurrently return to.

I hope these remarks may support you in your undertakings.

PERSONAL EXPERIENCES IN THE TREATMENT OF VESICOVAGINAL FISTULAS*

J. CHASSAR MOIR, OXFORD, ENGLAND

Nuffield Professor of Obstetrics and Gynaecology, University of Oxford, England

THE subject of my address is one of the oldest topics in gynecology—the vesicovaginal fistula. To say oldest topic is, perhaps, to put the cart before the horse; for it was the challenge of the vesicovaginal fistula that, in large measure, established gynecology as a specialty and, as every student of James Marion Sims knows, provided the stimulus for the creation of the earliest gynecological hospitals.

Having started on a historical note, I am much tempted to develop this theme, for there is a wealth of interesting material on which to draw. But the story of the vesicovaginal fistula has been told and retold; and on this count I myself am not innocent.¹ Let me turn instead to the purely practical side and discuss the operative treatment that I have found useful. By so doing I hope to contribute something constructive, something interesting and, I trust, something in keeping with the Joseph Price tradition.

Let there be no misunderstanding. The vesicovaginal fistula is today, in your country and in mine, a rare injury. Time was when a damaged bladder was the all-too-common consequence of a long, hard labor, or the result of ill-advised, or of unskillful instrumentation during labor. That type of fistula is now, fortunately, less and less common; although there are parts of Africa, India, and other undeveloped countries where it is still a major problem. But while obstetrical injuries lessen, injuries caused by gynecological surgery increase. And this is only to be expected, for the use of radical hysterectomy, of extensive vaginal plastic operations, and of radium therapy widens year by year.

Occasional injuries of the urethra, bladder, and ureters are therefore inescapable in modern gynecological practice. It is, however, true to say that no single operator is likely to see more than a very few such cases in his lifetime. It therefore follows that in most countries skill and experience in the repair of these injuries are hard to gain unless the operator goes out of his way to attract cases from a wider area than his own. This has been my position; and I have been fortunate in having many colleagues who, knowing my interest, have sent me cases from distant parts of the country, and sometimes from countries overseas.

As might be supposed, most of these referred cases have presented features of unusual difficulty; many of the patients had already been subjected to multiple previous operations; and not a few have been sent as "last resort" cases,

^{*}The Joseph Price Oration, presented at the Sixty-sixth Annual Meeting of the American Association of Obstetricians and Gynecologists, Hot Springs, Va., Sept. 8 to 10, 1955.

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before proceeding to that operation which, at a price, may give relief but which is no cure—I mean, transplantation of the ureters into the rectum, or into an isolated loop of intestine.

The 136 cases which I now present are, therefore, highly selected cases, selected because of their difficulty, their unusual nature, or because they had already resisted attempts at surgical closure. I emphasize this, for while a simple fistula may be successfully closed by many different methods, the real test for any technique is its reliability or adequacy in the difficult or complicated case.

TABLE I. VESICOVAGINAL FISTULAS

Obstetrical	42	(30.9%)	
Gynecological	94	(69.1%)	
Total	136	(100.0%)	

Rather less than one-third of my cases were obstetrical in origin. There were, as usual, two forms: those caused by tearing during operative delivery, and those caused by pressure necrosis after a long labor. The latter may not reveal themselves until several days after delivery; they are also the more difficult to treat, for there may be extensive loss of tissue around the bladder neck.

More than two-thirds of my cases were gynecological in origin, and the causes are listed in Table II. Because of the wide variety of causes there was, naturally, a wide variety of anatomical features. Those following hysterectomy were high in the vaginal vault, were often small, and were embedded in dense scar tissue. Those following colporrhaphy were low; and not infrequently the urethra, in whole or in part, had sloughed away leaving only a gutter. To digress for a moment, I think it is probable that in many of these latter cases the injury was not direct, but resulted from a hematoma which had become infected and had caused necrosis of the surrounding structures. In a few cases, unskillful catheterization after colporrhaphy may have been the cause.

TABLE II. GYNECOLOGICAL CAUSES OF FISTULA IN 94 CASES

CAUSE	NO.
Hysterectomy	
Abdominal or vaginal	38
Wertheim with or without radium	7
Removal of stump of cervix	1
Colporrhaphy (including "Manchester operation")	23
Radium	7
Congenital abnormality	3
Abdominoperineal resection of rectum (2 carcinoma; 1 granuloma)	3
Millin sling	3
Aldridge sling	2
Ulceration of obscure origin	2
Amputation of cervix	1
Myomectomy	1
Vaginal fixation	î
Cotton reel in vagina	î
Cystectomy after radium, with fistula of sigmoid colon	î

Experience in the preliminary examination of these patients has taught several important lessons. In not a few instances I have found that multiple



Fig. 2.—Large vesicovaginal fistula. The patient is in the knee-chest position, and the bladder is consequently ballooned out showing the blood vessels on the far wall.

Fig. 3.—Partial urethral destruction following colporrhaphy. Fig. 1.—High vesicovaginal fistula following hysterectomy. Two separate openings were present; the left one is barely visible in the photo-

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to ur pr fistulas were present. It is highly important that this possibility should be kept in mind, for a continuing leakage of urine from the undiscovered fistula may cause the patient to despair and to suppose that the operation for repair has been unsuccessful when, in fact, excellent union has occurred. Intravenous pyelography should always be performed to determine the state of the kidneys. A small opening high in the vagina and to one side of the midline should arouse the suspicion of ureteric rather than of bladder injury, and appropriate examination should therefore be made. Finally, in the preliminary examination the possibility of a bladder stone should be kept in mind; a phosphatic calculus readily forms in the bladder or in the upper part of the vagina in patients who have long-standing urinary leakage.

Types of Fistulas

Let me now depict some typical cases. But first I wish to mention an obvious fact. The most difficult cases of all—those with high, retracted fistulas -defy all attempts at photographic record. It follows that it is the low or easily accessible fistula that is successfully recorded by photography and which therefore finds its place in one's collection. By showing my pictures I do not therefore wish it to be supposed that the "Oxford" fistulas are, in comparison with those encountered elsewhere, picturesque rather than formidable.

In the first group of cases are the true vesicovaginal fistulas arising in the trigone of the bladder, usually in the midline (Fig. 1). Some of these were caused by difficult labor, but more were the result of injury during hysterectomy. A few followed the use of radium for careinoma of the cervix. If the fistula was large the ureters were sometimes exposed, even to the extent of displaying their rhythmic ejection of urine on the vaginal edge. Occasionally the ureter was grossly dilated; and I remember, in one case, being prompted by curiosity to insert the closed fistula scissors—to my astonishment the instrument passed upward with the greatest ease to the brim of the pelvis!

The second group consists of cases with bladder-neck destruction (Fig. 2). This was usually an obstetrical injury, and most often of the pressure-necrosis variety. In this class of injury the patient is much to be pitied for almost invariably she drips urine every moment of her existence and is denied even temporary relief by lying flat in bed. Some of these cases were most difficult to deal with for the reason that there had been extensive sloughing of tissue. Even if a good anatomical repair was achieved, functional recovery sometimes

lagged behind.

The third group concerns cases of urethral destruction (Fig. 3). Often (although this might not be obvious at first) there was also considerable damage to the so-called sphincter region of the bladder. This injury was sometimes caused by extreme difficulty in vaginal delivery, but oftener by a badly executed colporrhaphy or, as I have already suggested, by sepsis following a colporrhaphy.

Finally, there are the miscellaneous cases of ureterocervical fistulas, ureterovaginal fistulas, vesicocervical fistulas, radium necrosis of both bladder and rectum, and a variety of other disasters. I shall not attempt to discuss these in detail.

The Curability of Vesicovaginal Fistulas

No one doubts that every attempt should be made to bring about an anatomical repair of the fistula. Despite this obvious fact, an air of pessimism has unfortunately been allowed to surround this subject, and much too often the presence of some discouraging feature is taken as an excuse for transplanting

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the ureters into the colon or rectum. Now, this latter operation is far more dangerous than is generally realized. Jacobs,² in a recent review of more than 100 hospital cases, found that there was a mortality of no less than 12 per cent when the operation was performed in adults or elderly people. This risk should be clearly kept in mind by those who would resort to this method for the treatment of the nonmalignant fistula.

I should now like to comment on the features that are sometimes alleged to make plastic repair difficult or impossible.

The size of the fistula is no indication of difficulty in closure; indeed, some of the largest fistulas are surprisingly easy to close. Among my cases there have been those with openings that would admit two or even three fingers. There have also been cases with protrusion of the opposite wall of the bladder through the fistula, varying from a bulge seen on retracting the vagina to cases of complete inversion of the bladder so that the organ hung outside the vulva like a complete uterine procidentia (Fig. 4). In all these cases the fistula has

been successfully closed and function completely restored.

A complete destruction of the urethra is sometimes regarded as a hopeless injury. This, however, is not necessarily so; and even when there is associated bladder-neck destruction, the disability can often be overcome by a suitably designed reconstructive operation. Here I may mention that in this group I have been more successful in restoring complete functional control in my later cases than I was in one or two of my early cases. This I attribute to a more thorough building up of the muscular tissue of the bladder neck.

Previous operations undoubtedly make successful closure more difficult; but it is surprising how, with adequate exposure and careful technique, scar tissue can be excised and sound union obtained. Many of my cases were referred after multiple previous operations—8 or 9 or more (Table III)—yet I have been fortunate in each case in securing a closure.

TABLE III. PREVIOUS OPERATIONS (INCLUDING TRANSVESICAL AND TRANSPERITONEAL OPERATIONS)

NO. OF OPERATIONS	NO. OF CASES	
None	38	
1	34	
2	13	
3-5	27	
6-8	6	
9-11	3	
12	1	
17	1	
18	1	
19	1	
Not stated, or "many"	11	

Finally, the duration of the fistula has little relevance to its curability. In some of my cases there has been a urinary leakage for ten or more years (Table IV)—in one case it was for as long as 32 years—yet the bladder capacity after operation quickly returned to normal limits.

TABLE IV. DURATION OF FISTULA

YEARS	NO. OF CASES
Up to 7	117
8 to 10	6
11 to 20	4
21 to 24	7
28	i
32	î

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Much more important than any of the factors mentioned is an extensive destruction of the muscle of the bladder neck, or the presence of dense fibrosis around the fistula causing it to adhere to the ramus of the pubis. Either of these complications, if extreme, may make complete functional cure impossible. Despite this, substantial improvement can usually be obtained and the residual stress incontinence of urine, if present, is far less distressing than was the previous constant wetness.

Results of Treatment.—Regarding the results in 136 consecutive cases which I now present, I can state that closure of the fistula has been possible in all but 2 of the cases. The 2 possible exceptions were both cases of damage following radium treatment for carcinoma of the cervix. In one, a very slight leakage of urine persisted from a tiny hole high in the vagina, but I have not urged any further treatment. In the other there remains a ureteric leak after the repair of a combined bladder and rectal fistula caused by radium. I hope in the near future to attempt a reimplantation of the ureter into the bladder in this case.



Fig. 4.—Complete bladder inversion through a large vesicovaginal fistula.

Functional cure has usually been excellent but, as already mentioned, in certain types of cases there may be some residual stress incontinence. In 4 cases this was so troublesome that a transplantation of the ureters into the rectum was later recommended. Two of these patients suffered from extensive congenital abnormalities of the bladder, and, in retrospect, I think I was unwise to have attempted any plastic reconstruction. One of these patients declined any further operative treatment. In the 2 other cases of severe stress incontinence there had been an extensive destruction of the urethra and bladder neck. The transplantation operation, undertaken on the surgical side of the

hospital, was thus performed on 3 patients. In 2, the result was conspicuously successful, but I regret to say that in the third case the patient—an enormously stout woman—died after the operation. This is the only operative death in the entire series of vesicovaginal fistula cases.

I should like to emphasize the fact that these were the only 4 occasions in the 136 fistula cases, many of them previously regarded as "intractable," that the operation of transplantation of the ureters has been performed or advised. This experience should be contrasted with the statements sometimes made that the transplantation operation is necessary in a high proportion of cases; the deplorable figure of 90 per cent is even mentioned by one recent writer.

TABLE V. OPERATIONS REQUIRED TO CLOSE FISTULA

OPERATION	CLOSED AT FIRST OPERATION	CLOSED AT SECOND OPERATION	CLOSED AT THIRD OPERATION	CLOSED AFTER SIMPLE DRAINAGE
Repair of Vesicovaginal Fistula.— Had no previous operation	35*	1		
Had previous operation(s)	64	12	3†	3
Reconstruction of Urethra.—				
Had no previous operation	3	-	-	-
Had previous operation(s)	12	3	_	-

^{*}Includes case of previous resuturing attempted for reason of expediency 3 weeks after colporrhaphy.

†Includes 2 cases of radium necrosis.

Finally, I should like to remark that, with one exception, all fistula cases I have seen have been treated. The exception concerned an Irish woman with complete destruction of the whole anterior vaginal wall and with a doubly infected hydroureter. I doubt if local repair would have been possible, but I had no chance of putting treatment to test for the patient returned to her own country leaving no address behind. This is the only case in the entire series in which operative treatment has been withheld (cases with active carcinomatous growth excluded).

The Choice of Operative Approach

When an injury varies so much in character as does the vesicovaginal fistula, it is unreasonable to suppose that one operative technique will cover every type of case. Much also depends upon the training of the surgeon. The genitourinary specialist thinks in terms of the transvesical approach because of his familiarity with this method of operating; whereas the gynecologist prefers—even more strongly perhaps—the vaginal route. Yet again, there are bladder fistulas—those communicating with the pelvic colon for example—in which only the abdominal approach is possible. Having regard to these facts I cannot be dogmatic. Nevertheless I feel fully justified in pressing the claims of the vaginal route, and I do so for very strong reasons.

First, it is almost always practicable, and the exposure is at least as good as that usually obtained by the transvesical route. It is sometimes stated that a high vaginal fistula following hysterectomy is unsuitable for treatment from below. This statement is, in general, incorrect, for good exposure can almost always be obtained by making a generous episiotomy and using two or more pairs of Allis forceps as tractors. In only one case of true vesicovaginal fistula have I departed from the vaginal approach, and the necessity for so doing was not absolute.

Second, the vaginal approach permits a wide, raw surface of vaginal wall to be prepared for suturing; and this broad union is, I believe, far more effective than is the relatively feeble union obtained by stitching the bladder wall.

Third, if the operation is not successful, or not entirely successful, no great harm has been done, and further repair can still be contemplated. This cannot be said with equal truth of the abdominal or transvesical operations.

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To sum up, I can make my position clear if for a moment I indulge in exaggeration. I would say that the surgeon who chooses to approach a bladder fistula through the abdominal wall is the surgeon who would choose to remove the tonsils by digging through the structures of the neck instead of operating through the mouth.

Details of Operative Technique

I now propose to discuss in some detail operative technique for the repair of a fistula by the vaginal route.

Position and Exposure.—The patient may be placed in the knee-chest position or a modification thereof; or she may be placed in the lithotomy position. I have used both. The knee-chest position has a considerable advantage for a preliminary examination, especially if the patient is not yet anesthetized and can cooperate with the examiner. It is also useful for the operation itself, and very especially so if the fistula is retracted high under the pubic bone. Norman Miller of Ann Arbor, whose excellent work in repair of vesicovaginal fistulas is well known, routinely employs the inverted "jackknife" position which he has simplified by the use of a wooden frame to retain the patient in the desired position.

Despite these favorable remarks I find that for operative work I use the prone position less and less and I do not think I have employed it at all in the last 30 or 40 cases. There is sometimes difficulty in getting the patient into the required position and—especially if she is stout—in retaining her in that position. Furthermore, there is the very practical objection that blood tends to accumulate in the bladder and to form large, firm blood clots which may be very difficult to remove at the end of the operation, and which may seriously hinder subsequent bladder drainage. I have found the lithotomy position to be adequate in most cases, and exposure can be improved by slightly lowering the head end of the table.

Regarding retractors, the most serviceable is a medium, or small-sized Sims speculum. Occasionally, a small Auvard speculum is preferable. Sidewall vaginal retractors of the Wertheim type should always be at hand.

Four or five pairs of long Allis forceps are absolutely essential and are used for steadying the edges of a fistula, or for exerting traction to bring a high fistula within the operator's reach. For illumination a good spotlight is usually sufficient, but, exceptionally, a forehead light may be required.

Essential Instruments.—Other essential instruments are these. In place of the usual dissecting forceps the long, clip forceps for cleft-palate work is employed. A long-handled Bard-Parker knife with the No. 11 blade is used for all the dissection and is much superior in this class of work to the usual type of scalpel. Two stout scissors are included, one with the blade bent on the flat to an angle of 10 degrees, and one with the blade bent to an angle of 90 degrees. One or two long-handled hooks, both sharp and blunt, are frequently useful; and an assortment of small, well-curved needles, both cutting and round-bodies, must be available. A tubular sucker is invaluable for keeping the field clear of blood, and is preferable to the use of many small gauze swabs.

Suture Material.—I hold strong views regarding suture material, and I believe that many failures in this class of work are brought about by the use of too much, or of too thick, catgut. The operator should remember that the tissues around a fistula often have a poor blood supply, and that the wound itself is inevitably contaminated with urine. In these circumstances, catgut will provoke an exudate with risk of subsequent infection and necrosis.

When the fistula is small I omit the catgut altogether. In larger fistulas, or when the urethra has been reconstructed, I use only one row of very fine catgut, triple 0 in size, and restrict its use to the layer immediately adjacent to the bladder mucosa.

The main union is made by a broad approximation of the prepared vaginal walls and for this purpose interrupted stitches of monofilament nylon, No. 5 These are inserted mattress fashion to prevent an inrolling of the vaginal edges. They are left in position for at least three weeks by which time they begin to slacken, and their removal is then much easier than if it is attempted at an earlier date when postoperative edema is still present. Removal of the stitches does however call for care; and if the fistula is at a high level it is wise to undertake this part of the treatment in the operating theater with the patient anesthetized, and with the help of a good spotlight. I cannot approve of the practice, advocated in one recent article, of leaving unabsorbed sutures in position. On many occasions I have found phosphatic bladder calculi forming around unabsorbed sutures left by other surgeons, and the removal of these forgotten stitches has sometimes presented a considerable problem.

Operative Procedure.—In its simplest form, the operation I now perform consists of three main initial steps. First, the fistula is extended by incisions, through the vaginal wall only, upward from one margin, and downward from the other for a distance of one-third of an inch. Second, the vaginal wall is separated from the innermost edge of the fistula and undercut to the extent of about an eighth of an inch on both sides. Third, if the vaginal edges are scarred, or are unduly thinned by the undercutting, a strip of vaginal wall from one end of the preliminary incision to the other is removed by means of the The result in either case is a broad, beveled edge angled scissors (Fig. 5).

of raw vaginal wall which leads down to the bladder mucosa.

It is important that all epithelial remnants should be removed from around the fistula, but it is equally important that the bladder mucosa itself should not be excised for this adds nothing to the value of the operation but, on the contrary, makes the surgeon's work more difficult by reason of the uncontrollable oozing of blood that will be produced. In a satisfactory case, the slanting incision of the vaginal wall will show numerous tiny bleeding points; this indicates good vascularity and the prospect of sound union. If, however, scar tissue is encountered it is absolutely essential to continue the excision until vascular tissue is reached. The removal of the fibrous tissue is much helped by the use of the sharp hooks, particularly the right-angled hook, by which one can "feel" and pick up the suspicious areas on the raw vaginal edges.

At this stage it is wise to get in the deep row of fine catgut sutures. I use a running suture inserted in such a manner that the tissues immediately adjacent to the bladder mucosa are picked up, while the bladder mucosa itself is turned inward (Fig. 6). This may be a most time-consuming part of the operation, but it is essential that the stitching should be done accurately. The insertion of this row of stitches has a double function. Obviously, it brings together the deepest portions of the wound and so obliterates any dead space. But more important perhaps is its second function for, by keeping the innermost portions of the wound steady and firm, it enables the operator to return to the vaginal edges and to prepare them more thoroughly for the subsequent

stitching than he was able to do at the earlier stage of the operation.

The main stitching is now commenced, which, as already stated, consists of a series of nylon stitches inserted mattress fashion to bring the vaginal edges into broad apposition (Fig. 7). At one time, in accordance with the Marion Sims tradition, I employed silver wire, and was well pleased with the result. However, in more recent years, I have found that nylon stitches give an equally satisfactory result and are less troublesome than are silver wire sutures which so

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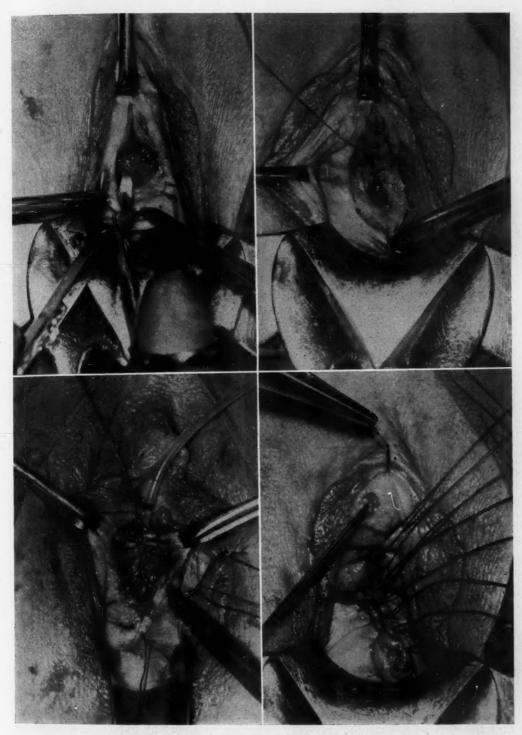


Fig. 7.

Fig. 8.

Fig. 5.—Repair of fistula (I). Large fistula is present at the vesicourethral junction. An incision has been made from the proximal margin of the fistula forward, through the vaginal wall; a similar incision (not seen) has been made from the distal margin. The vaginal edges are being excised with the 90 degree angled scissors (sometimes a No. 11 Bard-Parker knife is preferable).

Fig. 6.—Repair of fistula (II). The structures immediately over the bladder mucosa have been united with No. 000 catgut.

Fig. 7.—Repair of fistula (III). The main stitching with monofilament nylon has been started. One mattress stitch has been placed, another is being inserted.

Fig. 8.—Placing the silver wire anchor for the catheter. The nylon stitching has been completed and the relaxation incisions (if necessary) made. The wire suture is being placed deep through the tissues of the anterior lip of the urinary meatus, with a tubular needle. To the wire loop will later be tied the linen thread that holds the polyethylene catheter (it can be removed and replaced to the anchor at will).

easily kink or snap during manipulation. Each nylon stitch is clipped after insertion, and only after the last has been inserted are the individual stitches tied; by this means entanglement of the stitches, one with another, is avoided. Regarding the tying, the first cast when using nylon should always consist of a double turn; the second and third casts may be of one turn. Each stitch after tying is again clipped, and not until the last is tied are they cut. The ends are left at least one inch in length in order that they may be easily identified when the time comes for their removal.

A final and important step now awaits attention. With the repair completed there may be, in some cases, a dangerous tension in the neighborhood of the stitching. This is quite fatal to good results, partly because the stitches will cut out, and partly because the blood supply to the vaginal edges will be cut off and local sloughing occur. It is therefore essential that the surgeon should palpate the vaginal wall at the sides of the stitched line. If he encounters a tense ridge or ridges, he should divide the tissue with the scalpel. These relaxation incisions, on one or both sides, should be made parallel with the line of



Fig. 9.—Bladder drainage. The tube from the patient should not sag so much as is depicted, nor should the "drip" tube from the suction bottle be so long. (Reproduced from the Edinburgh Medical Journal 54: 368, 1947.)

repair, and as far to the sides of the vagina as is practicable. When this procedure is necessary the relaxation incisions will at once gape, and a new laxity will be found in the region of the repair. The relaxation incisions should be only one-eighth to one-quarter of an inch in depth; bleeding may be free at first but this soon subsides and seldom causes any real anxiety. The incisions rapidly epithelize in the next ten or fourteen days.

It will now be seen how the technique described differs from that advocated by most recent writers on this subject. The latter have usually advocated a very extensive separation of the vaginal walls in order that the bladder may be sutured free from tension. I dislike this method for the reason that it makes the operation unnecessarily extensive and, by creating thin vaginal flaps, it interferes in many cases with the blood supply and predisposes to infection and

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sloughing. Moreover, in some of the cases that one is called upon to deal with there is so much scarring with distortion that a wide separation of the vaginal walls from the bladder becomes virtually impossible; and in endeavoring to accomplish this technique the operator faces a serious risk of making the fistula worse than it was before.

Let us now return to the management of the fistula case after the repair. At the end of the operation the bladder must be thoroughly irrigated through a large-bore catheter connected to a Dakin rubber-bulbed syringe, in order to remove all blood clot. When it is certain that the bladder is quite free from all debris the catheter is stitched into position in the manner shown in Fig. 8.

I have now given up the use of rubber catheters for this purpose and instead use Portex tubing (a variety of soft polyvinyl tubing) which is far less irritating to the urethra, and which seldom causes trouble by becoming blocked by a deposit of urinary salts. Two or three extra eyes are cut in the end of the tubing, and the tube itself is carefully adjusted in length in order that it may reach well above the internal urinary meatus, but not extend so far as to irritate the wall of the bladder. I have no use for the self-retaining catheter, or for the Foley catheter, both of which in my hands have proved unreliable, and have caused much trouble.

Adequate bladder drainage is essential during the healing period. I use a simple arrangement of hydrostatic bottles to keep up a gentle suction (Fig. 9). Each day, or oftener, the bottles are disconnected and the bladder washed out by means of a Dakin syringe to ensure that the draining is kept free. After 14 days the catheter is removed and the patient is allowed to void urine naturally; this she should do every hour at first, and then gradually increase the interval.

As already mentioned, the nylon sutures are removed after a lapse of not less than 21 days.

Variations of Technique

In this description of technique I have, of course, pictured the easy, straightforward case. In practice there are innumerable difficulties to be overcomedifficulties which vary from case to case. I shall mention a few.

Sometimes it is necessary to cut through an occluding vaginal constriction in order to reach the level of the fistula. Whenever possible, this incision should be made in the posterior wall of the vagina, for any bleeding will then escape alongside the Sims retractor without obscuring the operative field. I have seldom found a Schuchardt incision necessary, but on many occasions I have performed a simple episiotomy either in the midline or, more frequently, slightly to one side of the vagina.

Sometimes it will be seen that tension will be less if the fistula is repaired from above downward—that is, repaired with the resulting suture line lying transversely in the vagina. It is always more difficult to introduce accurate sutures in this direction; but sometimes it is necessary. For introducing stitches in this "north-south," "south-north" direction I have found that the tubular needle technique is an advantage. To this end, I improvise by using a tonsilinjection needle which serves excellently for the purpose (Fig. 8).

If the fistula involves the anterior lip of the cervix, or if it is of the nature of a vesicocervical fistula, it will be necessary to separate the bladder from the cervix uteri. The bladder and the vaginal walls are then repaired independently of the cervix. Exceptionally, a portion of the anterior lip of the cervix may be used as a vascular structure to which the walls of the fistula may be united.

Regarding fistulas following hysterectomy, it is a very easy error to open the pouch of Douglas or, at least, to expose adherent loops of bowel. Great care must therefore be taken when placing the sutures in such cases.

Perhaps the chief danger in the repair of all high fistulas lies in the possibility of inadvertent injury to the ureter, or a kinking or strangulation of the ureter, by the stitches inserted during the repair. For this reason, great care must be taken in operating on a fistula which is situated high in the vagina and to one or the other side. It is a wise precaution in every fistula case to make a preliminary cystoscopic examination in order to determine the position of the fistula with reference to the ureters.

I have occasionally placed ureteric catheters in position before starting the repair, but despite theory, I have never found much help from their presence during the course of the actual operation. This, however, can be said in their favor. If there is real danger of the ureter being occluded, it is an insurance to have a ureteric catheter in position and to leave it in situ for the first six or seven days in order to ensure free drainage from the kidney. This lesson was learned from a case in which I found it necessary, in view of suspected ureteric obstruction, to perform a temporary pyelostomy. This operation at once relieved the patient of the painful sensations which she had had for the first two days after the fistula repair; fortunately, after the later removal of the vaginal stitches the free passage of urine into the bladder was at once restored.

In this connection I should like to add a historical note. The great Marion Sims, at the height of his fame, operated on a fistula case in London. It was the one and only occasion on which he performed the operation in my country. The patient died some days later, and it was discovered that one of his silver sutures had surrounded and obstructed both ureters. This was the first occasion on which Sims had committed this grave error. The publicity given to this case was unfortunate, for it had the effect of prejudicing British surgeons against Sims and his methods, and he was never given the full recognition that was accorded to him elsewhere.

Reconstruction of the Urethra

Since many of my cases have had a urethral reconstruction as the main feature of their surgical treatment I should like to say a special word about this type of case.

Sometimes the urethral defect is all too evident on the usual examination. Quite often, however, it is hidden by a loose bridge of vaginal wall left from the original injury, or from some previous inefficient reconstruction operation. Only if this bridge is retracted, or is snipped through, is the full extent of the damage revealed.

The first step in reconstruction is to place a thin polyethylene tube in position, stitching it to the tissues that will later form the external urinary meatus. This tube acts as a splint over which the new urethra is built, and also as a means of draining the bladder during convalescence. Next, the vaginal wall is incised from the apex of the urethral defect upward, to expose the neck of the bladder and to allow a later infolding of the muscle at this level.

The edges of what remains of the urethral gutter are now freed on both sides by a rather deep "stab" or "slit" incision made with the tapering Bard-Parker No. 11 blade; these incisions merge, as they pass upward, with the central incision already described. After a little further snipping with the angled scissors, the edges of the now mobilized urethral gutter are folded over the polyethylene tube by a running submucosal stitch of No. 000 catgut. Next, the bladder-neck area is reinforced by two or three separate, inrolling stitches of No. 1 catgut. Finally the main suturing is made by interrupted mattress sutures of nylon as for a vesicovaginal fistula repair. Any undue tension, if present, can be relieved in the manner previously described.

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Other Operative Methods

Almost all my discourse has concerned what might be termed the Marion Sims operation in modern guise. This is because I regard that operation as the method of choice in well over 95 per cent of the urinary fistulas that are today encountered in your country and in mine. Let me now briefly refer to certain other procedures.

Colpocleisis.—When, for good reason, the fistula itself cannot be repaired—and this usually means radium-treated cases—the possibility of vaginal closure or colpocleisis should be considered. If this operation will result in a big diverticulum of the bladder there is strong reason to advise against its use, for sepsis and stone formation will surely follow. Sometimes, however, the vaginal closure can be made at a high level where the diverticulum will be so small as to be almost nonexistent; and where any irregularity will be further smoothed out by the shrinking that occurs in the months after the operation. In this circumstance, the operation is reasonable; I have employed it on three or four occasions.

A circular ring of vaginal wall was removed immediately below the level of the radium fibrosis. The denuded area was then closed in layers, bringing the anterior vaginal wall into apposition with the posterior vaginal wall. The functional result of this operation has been surprisingly good, although one of my patients died some 18 months later from progressive low-grade infection of the bladder and surrounding tissues caused, apparently, by a late radiation reaction.

On only one occasion have I employed a low colpocleisis. That was the case of an unfortunate woman whose bladder had been removed for a malignant growth and whose ureters and pelvic colon had sloughed into what remained of the vagina. This patient was much relieved by the simple procedure of dividing in its entirety the rectovaginal septum, and closing the vaginal introitus; the rectal sphincter then served to control the passage of all excreta.

I am bound to confess, however, that I have found the operation of colpocleisis quite difficult, and in the case just mentioned I had to operate on three occasions before I was able to bring about a water-tight closure.

The Ingelman-Sundberg Operation.—Another remarkable case was that of a woman who, 12 years after radium therapy for carcinoma of the cervix, developed a bladder fistula. Examination showed an avascular vaginal vault covered with a superficial gray slough. Reparative surgery seemed quite impossible. On the advice of Dr. Ingelman-Sundberg, I carried out his ingenious operation of bringing new tissue with a good blood supply to the necrosed area. The gracilis muscle was isolated, turned upward with great care to preserve its blood supply, and brought through an opening in the obturator foramen to lie in the vault of the vagina. There it was tacked down around the fistula, in a prepared bed of denuded tissue. This procedure was remarkably successful, and restored to the patient almost complete continence of urine.

Combined Rectal and Bladder Fistulas.—When in addition to radium necrosis of the bladder there has also been a rectal fistula, I have dealt with the rectum first, after a preliminary iliac colostomy. The repair has been made on lines very similar to those detailed for the repair of a bladder fistula. Some six weeks after the removal of the stitches it has been possible to "undo" the colostomy; and, at a convenient later date, to undertake the bladder repair.

The Martius Operation.—If, after the closure of a low bladder or urethral fistula, there is only a thin layer of tissue to cover the suture line, some operators adopt Martius' technique of mobilizing the fat contained in the folds of the labia minora and using these pads as a buttress between the urethra and the vaginal walls. Alternatively, the anterior portions of the labia minora them-

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selves may be turned inward as a free graft. I have not myself used either of these methods, although Professor Scott Russell of Sheffield, who was previously my assistant in Oxford, tells me that he has used the latter technique with some success.

The Transvesical and Transabdominal Operations.—In my opening remarks I referred to the transvesical and transabdominal operations. I did so rather grudgingly for I am convinced that the prospect of cure is no higher than it is with the vaginal operation. One set of difficulties is replaced by another and, on the balance, the exchange is a poor one. It is not by the easy case that they should be judged, for that case is curable by many methods; rather it is by the case with bladder fixation, bladder retraction, and perivesical fibrosis. In these circumstances exposure by the transvesical route may be extremely difficult. Nor is the transperitoneal approach much better, for dense fibrosis between bladder and vaginal vault (here I refer particularly to the posthysterectomy case) may defeat the operator or, worse, may cause him to inflict yet more damage on the bladder and, possibly, on the ureters.

Now, I do not contend that there is no place for these operations—such an assertion would be absurd—but I maintain that their need is exceptional. In my own work I have used them only for the treatment of vesicocolic fistulas and, in one single case, for a resistant vesicovaginal fistula that was situated at an unusually high level in an unusually cicatrized vagina.

The Bastiaanse Operations.—At the recent Fourteenth British Congress of Obstetrics and Gynaecology, Professor Bastiaanse of Amsterdam demonstrated in cinefilm his remarkable operations. In certain cases of bladder fistula following radium necrosis he has extensively mobilized the bladder from the peritoneum of the anterior abdominal wall; by operating from below he has then pulled the fundus of the bladder downward to form a fold over the fistula. Not content with this repair, he has brought other vascular structures—a portion of the pelvic colon or even a mobilized segment of omentum—into the vaginal vault to interpose between the repaired bladder and the vagina.

I have no personal experience of such work although I admire the ingenious

and bold methods adopted by this outstanding Dutch gynecologist.

Ureteric Fistulas.—I cannot here discuss the operative treatment of ureterovaginal fistulas; suffice it to say that I have encountered several such cases; and when the ureteric injury has been combined with a vesicovaginal fistula I have included them in the series presented in this paper.

Summary

I can best round off my address by listing do's and don'ts which summarize my main thoughts upon the problem of the vesicovaginal fistula.

Don't despair of local closure of a vesicovaginal, or urethrovaginal, fistula. The great majority can be repaired by simple, direct methods.

Don't attempt a transvesical or transabdominal operation, nor an extensive flap-splitting or grafting procedure, unless for very special reason.

Don't use catgut for the repair unless it is of a very fine variety and is restricted to the tissues immediately adjacent to the bladder or urethral mucosa. Monofilament nylon is the best suture material for the vaginal wall.

Don't forget to clear out all blood clot and debris from the bladder at the end of the operation, and to maintain constant drainage for fourteen days.

Do make sure that there is no tension on the stitches at the end of the operation. If tension is present do not hesitate to make a relaxation incision on one or on both sides.

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Do make sure that there is not a bladder stone present.

Do be careful of the ureters during repair.

Concluding Remarks

The vesicovaginal fistula is, in the great majority of cases, an eminently curable lesion. But it must be treated with respect. If it is easy of access and is surrounded by soft, vascular tissue, its repair can be confidently undertaken by any operator well experienced in vaginal plastic surgery. If, however, the fistula is not of this simple type, there should be no hesitation in placing the patient in the hands of a surgeon who has had experience in this very specialized work.

Success in fistula repair demands from the surgeon good eyesight, gentleness of touch, and an unwavering attention to the minutiae of technique. Above all, it requires infinite patience: if he must hurry he should not start. But his reward is great. There is no patient more sincere in her gratitude than the woman whose seepage has been stopped, and who has been restored to her rightful activity in the midst of her family.

I wish to thank the Committee of the First Gynecological and Obstetrical Congress of Venezuela for kind permission to incorporate in this paper certain matter which was presented to their Congress in January, 1955.

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PUERPERAL VASOMOTOR COLLAPSE IN PATIENTS WITH TOXEMIA OF PREGNANCY—A NEW CONCEPT OF THE ETIOLOGY AND A RATIONAL PLAN OF TREATMENT*†

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VASOMOTOR collapse is a serious though infrequent complication of the toxemias of pregnancy and usually appears within the first twenty-four hours following delivery. Because of the relative rarity of this complication, its basic nature has remained poorly understood and only empiric therapy has been proposed and employed.

Bailey¹ in 1911 reported the first series of cases of this shocklike state and attributed the profound shock and drop of blood pressure to rapid emptying of the uterus of the eclamptic patient. Veratrum viride had been used in 4 of his 6 patients, and he considered that the effects of this drug were contributing factors to the production of shock. Schwarz² reported 10 additional cases manifesting this shocklike state following delivery. He did not use veratrum as a hypotensive agent, but attributed the state of collapse to great splanchnic vascular dilatation resulting from the abdominal decompression incident to delivery. He felt that a pooling of blood in the splanchnic area resulted in insufficient filling of the right ventricle of the heart with resulting systemic hypotension. With this concept of the condition, he logically recommended the use of sand-bags and tight abdominal binders; and, in addition, he administered epinephrine and pituitary extract. Schwarz also observed that this shocklike state was distinct and separate from the usual condition of vascular collapse resulting from a severe loss of blood. He correlated the "nephritic" toxemia and postpartum shock. Simons and Rasmussen in 1925 observed that in normal pregnant women there was a rapid increase in blood pressure during labor followed by a marked decrease after delivery, and then a gradual additional decrease to normal pressures within six weeks after delivery. They also observed that these changes were often markedly exaggerated in the toxemic patient. Adair, Hunt, and Arnell in 1936 summarized the literature on this subject and described in addition 26 cases of their own. They concluded that toxemia was the most important etiological factor, with delivery precipitating the onset of the vascular collapse. They also observed that in those patients who failed to survive this crisis, the most common pathologic lesion was that of chronic glomerulonephritis. They reported an over-all mortality rate for this type of collapse of 15.49 per cent.

^{*}Aided in part by the Edward G. Schlieder Educational Foundation of New Orleans, Louisiana.

[†]The Foundation Prize Thesis, presented at the Sixty-sixth Annual Meeting of the American Association of Obstetricians and Gynecologists, Hot Springs, Va., Sept. 8 to 10, 1955.

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Additional facts concerning the pathology of this serious complication have been observed and reported herein by the authors. These facts and some of the therapeutic implications resulting from them constitute the present preliminary report.

Routine determinations of serum sodium, potassium, and chloride were performed on most of the toxemic patients admitted to the Louisiana State University division of the obstetrical service of Charity Hospital of Louisiana at New Orleans. In many instances several determinations were performed on the same individual at different phases of her disease. In 1952 the first serum electrolyte determinations were performed in this laboratory on a patient at a time coinciding with the appearance of the postpartum vascular collapse. The sodium concentration in the serum of this patient was 112 meq. per liter. This markedly low concentration suggested that perhaps the development of vasomotor collapse was associated with or at least related in some way to the altered sodium metabolism known to be present in patients wih pre-eclampsia or eclampsia. At the time this present report was prepared, 8 toxemic patients had had determinations of serum electrolytes done coincidentally with the presence of postpartum vasomotor collapse. The electrolyte analyses were done as described in an earlier report by one of us, H. J. T.⁵

In view of the apparent coexistence of vasomotor collapse and low serum sodium and high serum potassium concentrations in these patients, a crude working analogy was drawn between this "shocklike" state and the collapse state which is described as an Addisonian crisis.

In order to pursue this analogy, it was decided to evaluate the effects of intravenously administered solutions of sodium chloride upon these patients. This decision was made with considerable apprehension inasmuch as Dieckmann⁶ and others have demonstrated the deleterious effects of excessive amounts of sodium chloride on certain toxemic patients. Also, the time interval required for the determinations of the serum electrolyte concentrations (averaging 3 hours in this laboratory) made it mandatory that definitive therapy be instituted long before the original electrolyte concentrations could be ascertained.

An arbitrary therapeutic regime was established for all toxemic patients on whom a clinical diagnosis of vasomotor collapse was made following de-These steps were taken in the following order: A sample of whole blood was obtained, with proper precautions necessary for accurate electrolyte Blood loss estimated to be 500 c.c. or more was replaced determinations. immediately by transfusions of donor's blood. An aqueous solution of sodium chloride was administered intravenously to the patients who had had no significant blood loss and to those patients whose estimated excessive blood loss had been replaced without effecting a reversal of the collapse state. instances 3 per cent solutions of sodium chloride in water were administered while 0.9 per cent solutions of sodium chloride were given to the remaining patients included in this study. Frequent determinations of blood pressure, pulse rate, and general clinical conditions were made during the period that the salt solution was being given. Another specimen of blood for electrolyte determinations was drawn approximately 20 minutes after the completion of the sodium chloride infusion. A third blood specimen was obtained 10 to 13 hours later. Routine serum electrolyte concentrations in toxemic patients during labor and at varying intervals during the immediate puerperium provided the control levels used for purposes of comparison. These are not ideal controls, but are the most comparable data available. The clinical classification of the patients in both groups is comparable. A comparison between the serum electrolyte concentrations of patients who manifested collapse and at comparable times of toxemic patients who did not manifest collapse is shown in Table I. In one patient only (L. H.), two serum electrolyte determinations were made prior to the collapse. The first was done early in labor, approximately 20 hours prior to delivery; whereas, the second was done approximately 2 hours after delivery and 9 hours prior to the onset of collapse. In this one instance there occurred a fairly rapid and marked decrease in serum sodium concentration preceding the appearance of vascular collapse.

TABLE I. INTERVAL SERUM ELECTROLYTE CONCENTRATIONS IN TOXEMIC PATIENTS

	NO.	MEAN EL	ECTROLYTE CON (MEQ./L.)	CENTRATION
	PATIENTS	Na+	K+	Cl-
Patients Manifesting Collapse.—				÷ .
Prior to collapse (patient L. H.) (during labor) 20 hours before delivery 2 hours after cesarean section	1	133.7 125.9	3.48 3.57	102.6 102.1
During collapse (6-9 hours post partum)	5	120.0 (112.3-128.4)	5.69 $(5.15-6.22)$	94.6 (93.7-102.1)
After collapse (20-24 hours post partum)	5	133.8 (131.2-136.0)	4.73 (3.86-5.37)	101.5 (96.0-106.3)
Patients Without Collapse.—				
During labor	26	135.9 (126.9-140.1)	4.3 (3.34-5.46)	$103.3 \\ (96.3-110.7)$
Post partum (1-9 hours)	14	134.5 (132.0-138.8)	4.58 $(3.96-5.43)$	101.1 (98.7-108.7)
Post partum (10-24 hours)	20	136.2 (130.9-143.5)	4.5 (3.64-5.10)	102.8 (95.1-107.7)

TABLE II. INDIVIDUAL SERUM ELECTROLYTE CONCENTRATIONS IN PATIENTS WITH PUERPERAL TOXEMIC VASOMOTOR COLLAPSE. (MEQ./L.)

PA-	Co	llapse St	ate	A	fter Na	Cl	12	Hours L	ater
TIENT	Na+	K+	Cl-	Na+	K+	Cl-	Na+	K+	Cl-
L.D.	-			130.0	4.68	88.8	135.2	5.37	96.0
E. A.	112.3		80.0	130.1	6.85	99.5	132.5	5.07	99.1
G. W.	121.9		97.0	125.4	-	98.0	136.0	_	100.0
G. C.	128.4	5.15	102.1	133.9	4.61	106.9		-	-
L. H.	122.2	-	100.0	128.2	Generalists.	106.9	131.2	3.86	106.3
G. P.	115.3	6.22	93.7	130.4	5.66	105.8	134.1	4.63	106.3
Mean	120.0	5.69	94.6	129.7	5.45	101.0	133.8	4.73	101.5

It is apparent from the data presented in Table I that, although the number of patients manifesting collapse is very small, not only is their mean serum sodium concentration much lower than that of comparable controls, but also that there is no overlapping of the range of concentrations. The mean concentration of serum sodium of 5 patients during the height of the collapse state was 120.0 meq./L. with a range of 112.3 to 128.4 in contrast to a mean of 134.5 meq./L. found in the control series. The mean potassium concentration in the collapse series was 5.69 meq./L. in contrast to 4.58 meq./L. found in the noncollapse controls. There was no overlapping of the range of these two series. The chloride concentrations of the collapse series was 94.6 meq./L.,

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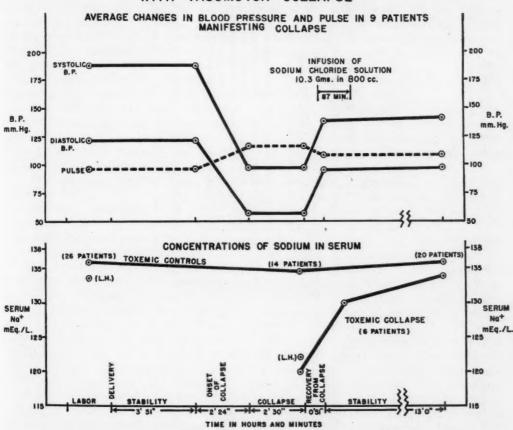
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and of the controls was 101.1 meq./L. There is an overlapping of the range of these two series. The results of the individual serum electrolyte determinations on 6 patients who manifested postpartum collapse are listed in Table II. In only 2 instances were potassium determinations obtained during the collapse period because of failure to separate the serum from the red cells within one hour after the blood had been drawn. Failure to separate the cells from the serum permits lysis of a certain number of red blood cells with a resulting artifactitious increase of the serum potassium concentrations. Sodium concentrations, on the other hand, are not significantly altered by even moderate degrees of hemolysis inasmuch as the red cells contain minimal quantities of sodium.

EFFECTS OF SODIUM CHLORIDE UPON TOXEMIC PATIENTS WITH VASOMOTOR COLLAPSE



It is important to note that serial electrolyte concentrations were obtained on the patients who manifested collapse, whereas the control determinations were in most instances made upon different patients in each of the three time intervals. The effects of the intravenous administration of a solution of sodium chloride to patients in collapse are illustrated graphically in Fig. 1. In this figure, the mean changes in blood pressure, pulse rate, and serum sodium con-

Fig. 1.

Although the average time after delivery that collapse occurred was 6 hours and 15 minutes, the variation among these 9 patients was between 15

centration during the various intervals under investigation are presented.

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TABLE III, CLINICAL DATA ON PATIENTS WHO MANIFESTED COLLAPSE

PATIENT	RACE	AGE	GRAVIDITY	WEIGHT	TYPE OF TOXEMIA	TYPE OF DELIVERY	ESTIMATED BLOOD LOSS	ANESTHESIA
F.T.	Negro	39	Δ.	161	HCVD + pre-eclampsia	Spontaneous	<150 c.c.	None
J. D.	Negro	22	VII	707	HCVD + pre-eclampsia	Spontaneous	(500 c.c. replaced)	None
G.C.	Negro	43	xviii	218	HCVD + pre-eclampsia	Spontaneous	150 c.c.	None
L.D.	Negro	39	X	200	HCVD + pre-eclampsia	Spontaneous	200 c.c.	None
E. A.	Negro	44	vii	215	HCVD + pre-eclampsia	Cesarean section	350 e.e.	Local infiltration
L. H.	Negro	44	vi	220	HCVD + pre-eclampsia	Cesarean section	400 e.e.	Local infiltration
	Negro	21		Not recorded	Pre-eclampsia .	Spontaneous	<150 c.c.	None
G. W.	Negro	20	. per	133	Pre-eclampsia	Midforceps	500-700 e.e.	Local infiltration
)					(traumatic)	(500 c.c. replaced)	(pudendal block)
G. P.	Negro	55	٠,	110	Pre-eclampsia	Cesarean section	300 c.c.	Local infiltration
							(300 c.c. replaced)	

minutes and 24 hours. The duration of the collapse present in these 9 patients ranged from 40 minutes to 8 hours and 10 minutes with an average of 2 hours and 30 minutes. Restoration of vessel tone with a return of the blood pressure to stable levels occurred in all 9 patients coincidentally with the administration of the solutions of sodium chloride. Each patient received an average of 10.3 Gm. of sodium chloride in approximately 800 c.c. of water. The mean time required for the administration of the salt solution to this group of patients was approximately 87 minutes. Recovery from the collapse state was observed on an average of 51 minutes after the saline injection was started. During this time, approximately 7 Gm. of sodium chloride had been administered in an average volume of 500 c.c. of water.

The average precollapse blood pressure was 187 mm. Hg systolic and 121 mm. Hg diastolic. During the collapse the blood pressures averaged 97 mm. Hg systolic and 57 mm. Hg diastolic. There was an average increase in the pulse rate from 96 per minute prior to the collapse to 116 per minute during the collapse. Clinical recovery from the collapse was associated with an increase in the blood pressure to an average of 138 mm. Hg systolic and 95 mm. Hg diastolic. There was a simultaneous decrease in pulse rate to 108 per minute. During the subsequent 13 hours after recovery from the collapse, an average blood pressure of 141 mm. Hg systolic and 97 mm. Hg diastolic was maintained with no additional therapeutic aids.

The administration of solutions of sodium chloride to the patients in collapse was associated with an increase of the serum sodium concentration from 120.0 meq./L. to 129.7 meq./L. An additional increase up to 133.8 meq./L. occurred within the following 10 to 13 hours. During this time. no additional sodium chloride had been given.

The clinical data on each of the patients who manifested collapse are listed in Table III. Five of the 9 patients were 39 years of age or older. Six had been pregnant 5 or more times. Five patients weighed 200 or more pounds at the time of labor. Six patients had pre-existing hypertension with superimposed pre-eclampsia. The remaining 3 patients had pre-eclampsia alone. Three patients were delivered by means of cesarean section. One patient was delivered by a traumatic midforceps procedure. The remaining 5 patients were delivered spontaneously. The estimated blood loss at the time of delivery for each of these 9 patients ranged from less than 150 c.c. to 700 The two patients who lost approximately 700 c.c. of blood were given c.c. of whole blood immediately after the blood loss occurred. In each of these patients the severity of collapse was out of proportion to that which would ordinarily be attributed to the amount of blood lost. Five patients were delivered spontaneously without any anesthetic. Local infiltration anesthesia with 1 per cent solutions of procaine hydrochloride was used for each of the three cesarean sections. Pudendal block and local infiltration with a solution of procaine hydrochloride were employed for the midforceps delivery. In each instance where procaine was used, the patients were given 120 to 300 mg. of phenobarbital premedication.

In addition to the 9 patients upon whom detailed controlled observations have been made, we have recommended the use of intravenous solutions of sodium chloride for 7 additional patients who manifested the same collapse syndrome. Sodium concentrations in the serum of 3 of these patients (E. J., T. P., R. P.) were determined prior to the administration of saline solutions. These concentrations were 113.0, 125.3, and 108.5 meq./L., respectively. All 7 of these patients had failed to respond to blood transfusions and solutions of glucose. In each instance marked clinical improvement was apparent during and following the administration of the solutions of sodium chloride. One

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of these patients (R. P.) had eclampsia and her pregnancy had been terminated by a cesarean section. Vascular collapse occurred immediately after operation. After the estimated blood loss had been replaced without significant response in blood pressure, levarterenol bitartrate (Levophed*) was given by the intravenuos drip method. Satisfactory elevation of the pressure was attained with considerable difficulty. An attempt to decrease the rate of administration was met with a return of the blood pressure to shock levels. At this time the serum sodium concentration was 108.5 meq./L. Two hundred cubic centimeters of a 3 per cent solution of sodium chloride was administered rapidly. There was marked improvement in the clinical appearance of the patient, and administration of levarterenol bitartrate was no longer necessary to maintain a satisfactory blood pressure.

The sodium concentration in the serum had increased to 112.9 meq./L. twenty minutes after the saline infusion was completed. Twenty-four hours later, without additional sodium chloride, the serum concentration had increased to 129.2 meq./L.

There were no deaths in this entire series of 16 cases.

Comment

Vascular collapse occurring in the toxemic patient during the first 24 hours following delivery has been mentioned but infrequently in the literature, and has been generally neglected by the investigators interested in the basic factors initiating or contributing to the deranged physiology present in the toxemic patient.

A careful study of the serum electrolyte concentrations at the height of the vascular collapse permits an analogy to be drawn between this type of collapse and that associated with acute adrenal insufficiency or Addisonian crisis. In both conditions serum concentrations of sodium and of chloride are very low, whereas potassium concentrations are increased. nations for the deficiency of sodium in the blood in these two conditions are, however, very different. In Addison's disease, there is, among other things, a deficiency of the sodium-retaining corticoids, thus permitting excessive loss of sodium by the kidneys. In toxemia of pregnancy on the other hand, there is an excess of sodium-retaining corticoids according to Chart, Venning, and others. These corticoids apparently cause a shift of sodium out of the vascular system into the extravascular intra- and extracellular compartments. This shift of sodium out of the vascular compartment has been demonstrated by Tatum⁵ with the observation that the serum concentrations of sodium in pre-eclamptic patients were significantly below those found in normal pregnancy, and that in the toxemic patient the edema fluid contained a higher concentration of sodium than did the respective serum. A positive sodium balance associated with a decreased rate of excretion of sodium by the kidney has been repeatedly demonstrated in pre-eclamptic and eclamptic patients.

In Addison's disease, a crisis may be precipitated by stress factors such as surgery, loss of blood, or infection. It is well known that the patient with Addison's disease tolerates the stresses of pregnancy rather poorly. Brent's reviewed 40 cases of Addison's disease complicated by pregnancy, and con-

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cluded that the crisis associated with vasomotor collapse was a common major hazard and was most frequently encountered during the puerperium. She suggested that "the stress and strain of labor and the blood loss coupled with the cessation of fetal adrenal secretion and a decrease in the titer of the circulating sex hormones may possibly be the reason for the development of crisis during this period." Vascular collapse in the toxemic patient is prone to occur following an operative delivery such as a cesarean section or a forceps delivery. The collapse may occur at any time within 24 hours after the inciting stress. It has also been observed in the toxemic patient after intrauterine death of the fetus but prior to labor and delivery.

If credence is to be placed on the theory that the vasomotor collapse in the puerperal toxemic patient is to be explained by an acute adrenal cortical failure, one should be able to establish or at least explain in theory the preexistence of a relative degree of adrenal insufficiency. The investigations of Johnson and Haines11 have indicated that there are substances in human placental tissue having adrenal hormonal activity. Lloyd and associates, 12 as well as Venning and co-workers,8 and others have presented data which strongly suggest that there is an increased production of adrenal corticoids associated with pre-eclampsia. These reports support the theory that the placenta may well be an active steroid-producing organ, and that this activity may be markedly increased in patients who have pre-eclampsia. These exogenous corticoids could effect suppression of the adrenal cortex in a manner similar to the action of cortisone as reported by Salassa and collaborators, 13 who observed that cortisone therapy was occasionally followed by atrophy of the Fauvet and Münzner¹⁴ reported that the adrenal glands adrenal glands. removed from 6 patients who had died of eclampsia were markedly atrophic. These reports lend support to the assumption that in some toxemic patients there may develop a relative degree of adrenal cortical insufficiency shortly after delivery.

It may be of interest to speculate on the actual significance of low concentrations of sodium in the serum. Sodium concentrations as low as or lower than those found at the height of the collapse have been observed in pregnant patients without associated vascular collapse. These patients, however, did not have pre-eclampsia. It would seem to be unlikely that the vasomotor collapse observed in the toxemic patient could be explained entirely on the basis of acute sodium deficiency as described by Elkinton and associates15 in experimental animals. It is perhaps significant that puerperal toxemic vascular collapse occasionally occurs in patients who have been hospitalized for several days because of their toxemia, or who have been unusually conscientious in adhering to their physician's admonitions regarding the restriction of salt. A reduction in the intake of sodium chloride undoubtedly can contribute to the development of a low sodium concentration in the serum. This factor, however, is in all probability much less important in the production of vascular collapse than is the abnormal shift of sodium from the vascular compartment into extravascular intra- and extracellular spaces which is associated with pre-eclampsia.

In most pre-eclamptic patients, there occurs a rapid mobilization of extravascular water within a short time after delivery. This phenomenon is made apparent clinically by the rapid disappearance of edema, by the occurrence of hemodilution, and by the significant increase in urinary volume. The data presented in this report indicate that there occurs a rapid mobilization of extravascular sodium and chloride associated with the mobilization of water. This is evident from the observations that the serum concentrations of sodium and of chloride continued to increase toward normal even after the administration of sodium chloride had been completed. These increases in serum concentrations of sodium and of chloride occurred quite rapidly, and were not dependent upon an increase in the total quantity of sodium and of chloride in the body. It seems logical to assume that mobilization of sodium with the resulting increase in its concentration in serum may prevent, in many instances, the development of puerperal toxemic vascular collapse, and may explain the occasional "spontaneous" recoveries observed in these patients.

In view of the data presented in this report, it is not unlikely that one of the principal causes of death in the toxemic patient may be vasomotor collapse resulting from a combination of low concentrations of sodium and of chloride in the serum and some degree of adrenal cortical insufficiency. Additional data will be required before the relationship of the adrenal cortex to the development of puerperal vasomotor collapse may be clearly understood.

The coexistence of a low concentration of sodium and a high concentration of potassium in the serum and the appearance of vasomotor collapse in the toxemic patient has been demonstrated for the first time. On the basis of these observations, solutions of sodium chloride in water were administered intravenously as specific therapy for this complication. The results were completely gratifying in each of the sixteen patients treated in this manner. The sodium chloride did not produce any apparent deleterious effects in these patients.

Although the series of patients presented in this report is too small to permit statistical analysis, the survival of all of the patients treated appears to be in sharp contrast to the high mortality associated with this condition reported by others and observed by us prior to this investigation.

Summary and Conclusions

Vasomotor collapse developing in the toxemic patient during the first twenty-four hours of the puerperium has been studied with particular emphasis upon electrolyte metabolism.

Serum concentrations of sodium, potassium, and chloride have been determined on eight patients coincidentally with the presence of vascular collapse. The sodium and chloride concentrations were very low in every instance. The concentrations of potassium were increased above the control values. The clinical as well as chemical similarity of this condition to vasomotor collapse resulting from acute adrenal cortical insufficiency suggested the use of sodium chloride as a specific therapeutic agent.

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Sixteen patients have been treated with either hypertonic (3.0 per cent) or isotonic (0.9 per cent) solutions of sodium chloride in water. The intravenous administration of one of these solutions of sodium chloride was followed in each instance by a prompt and often dramatic recovery from the state of vasomotor collapse.

There were no deaths in this series.

We wish to express our gratitude to Misses Orris Hall and Frances Arrighi for their valuable assistance in the preparation of this paper.

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URINARY TRACT INJURIES RESULTING FROM PELVIC SURGERY*

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COMPLICATIONS resulting from injury to some portion of the urinary tract have been among the more serious hazards of gynecological surgery since the very beginning of such surgery. Radical hysterectomy for carcinoma of the cervix has always been thought of as the type of operation most likely to lead to such injury, but experience over the years has shown that this is by no means the only type of operation during which such injuries may occur. The removal of large pelvic masses, particularly those of an inflammatory nature, or of intraligamentary fibroids or cysts often entails dissection, clamping, and ligating very close to the ureters or bladder; and in such cases it is only by the most meticulous care that injury to these structures can be avoided.

In earlier years Sampson¹ reported 32 ureteral injuries during the first thirteen years of the Johns Hopkins Hospital, and 19 of these occurred during operations for cervical cancer. During the same period 4,086 major operations were performed, 139 of which were for cervical carcinoma, so that the incidence of ureteral injury in the surgical treatment of this disease was 14 per cent. Bland² found 25 ureteral injuries, or 19 per cent, in a series of 139 operations for cervical cancer, and quotes Wertheim as having reported an incidence of 49 injuries during 500 hysterectomies, or approximately 10 per cent. Liu and Meigs,³ in the latest report from Meigs' clinic of 473 patients subjected to the radical hysterectomy and pelvic lymphadenectomy, report 45 fistulas of all types, or an incidence of 9 per cent. In all but 4 of these cases, in some of which multiple fistulas developed, some portion of the urinary tract was involved.

We have felt that an analysis of urinary tract injuries resulting from a variety of gynecological operations, occurring and/or treated on our service during the 21 years 1933 to 1953, inclusive, might be a worth-while addition to the published data on this subject. During this period certain significant changes have taken place in our surgical procedures. The subtotal hysterectomy for benign pelvic disease has been largely replaced by total hysterectomy, vaginal hysterectomy has been performed with steadily increasing frequency, and in the later years radical surgery for malignant conditions, especially carcinomas of the cervix, has been revived in a limited number of selected cases.

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The material to be presented consists of the following:

Ureteral injuries, 40 cases.

^{*}Presented at the Sixty-sixth Annual Meeting of the American Association of Obstetricians and Gynecologists, Hot Springs, Va., Sept. 8 to 10, 1955.

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Perforation or incision of the bladder recognized and repaired at the time, 77 cases.

Vesicovaginal fistulas, 56 cases.

Ureteral Injury

The ureteral injuries have been divided into three groups as follows:

A. Injuries recognized and repaired at the time of occurrence, 19 cases. B. Injuries occurring during surgery at the Johns Hopkins Hospital, but only recognized and repaired later, 12 cases.

C. Injuries occurring elsewhere but repaired on our service, 9 cases.

In Table I may be seen the types of conditions for which the surgery resulting in these injuries was performed for all three groups. While uterine fibroids is the most frequent single diagnosis, the frequent presence of adhesion-producing conditions such as pelvic inflammatory disease or endometriosis is of definite significance. Carcinoma of the cervix appeared twice in each of the three groups, an incidence of 15 per cent.

TABLE I. TYPES OF CONDITIONS FOR WHICH SURGERY RESULTING IN URETERAL INJURY WAS PERFORMED

DIAGNOSIS	A	В	C
Myomas of the uterus with severe pelvic inflammatory disease	7	7	2
Myomas of the uterus with severe pelvic inflammatory disease plus cervical and intraligamentary nodules Myomas of the uterus plus endometriosis	1		
Endometriosis	1		1
Endometriosis plus carcinoma of cervix, International Classification, Stage 0	,		
Carcinoma of cervix, International Classification, Stage 0 Carcinoma of cervix, International Classification, Stage I,	1	1	
post irradiation	1	1	2
Ovarian or pelvic cysts with adhesions	4		
Carcinoma of ovary, bilateral	1		
Carcinoma of endometrium		1	
Sarcoma of cul-de-sac, recurrent	1		
Ruptured uterus at term		1	
Degenerated fibroma of ovary		1	
Postabortal broad ligament abscess			1
Diagnosis not definitely known			3
Total	19	12	9

TABLE II. OPERATIONS

	A	В	C
Subtotal abdominal hysterectomy with bilateral or unilateral adnexectomy	10	1	
Total abdominal hysterectomy with bilateral or unilateral			
adnexectomy	1	9	5
Modified Wertheim hysterectomy	2	1	
Radical Wertheim hysterectomy	1	1	
Modified posterior exenteration	1		
Removal of adherent cysts	3		1
Excision of endometriosis of left ovary and cul-de-sac	1		
Vaginal hysterectomy			1
Abdominal removal of cervical stump			1
Incision of broad ligament abscess			1
Total	19	12	9

The types of operations performed in the three groups are shown in Table II. A significant observation to be made from this table, it appears, is the

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fact that unrecognized injuries occurred much more frequently in the course of total hysterectomies than when more conservative procedures were being done. Six of the 31 ureteral injuries which occurred during surgery performed at the Johns Hopkins Hospital, 4 recognized and 2 unrecognized, occurred during radical surgery for malignant disease. As this type of surgery represented a very small proportion of the major surgery performed during the period, these 6 injuries, essentially 20 per cent of the total 31 injuries, reemphasize the high potentiality of ureteral damage during this type of surgery.

That experience of the surgeon constitutes no valid insurance against such injury is borne out by the fact that 15 of the 31 operations in which such injuries occurred at the Johns Hopkins Hospital were performed by members of the visiting staff and 16 by members of the resident staff.

TABLE III. TYPES OF URETERAL INJURY OR RESULTING DEFECT

	A	В	C
Transection	12		
Laceration	3		
Catheter perforation	3		
Ligation, unilateral	1	1	
Ligation, bilateral		1	
Stricture, impassable			1
Ureterovaginal fistula		10	8
Total	19	12	9

In Table III may be seen the types of ureteral injuries encountered. The presence of 3 catheter perforations resulting from preoperative catheterization of the ureters might be considered as an argument against this procedure. This is a relatively small incidence of this type of injury, however, when we consider that this procedure has been carried out for all Modified Wertheim operations, now approximately 250 cases, and in many other cases of severe pelvic inflammation or endometriosis in which technical difficulties were anticipated. In one of these 3 the perforation healed without specific treatment, in another with no treatment except extraperitoneal drainage to the site of the perforation, while in the third the injury was sufficiently extensive to lead the operator to perform a ureterovesical anastomosis. As previously shown by one of us,⁴ ureteral perforation frequently occurs during the practice of cystoscopic examinations or treatment, and rarely requires treatment other than careful observation with sulfonamide or antibiotic therapy.

We firmly believe that in anticipation of such difficulties as we have mentioned the preoperative insertion of catheters into the ureters is a wise precaution, but we cannot agree, as recently suggested by Aschner,⁵ that it should be done routinely preceding all major pelvic surgery. We feel that a sound training in urology and thorough familiarity with the anatomy of the urinary tract on the part of those surgeons who operate in this region is of more fundamental value.

Treatment

Reference to Table IV will show that our treatment of choice for the more severe ureteral injuries and for those resulting in ureterovaginal fistulas has been ureterovesical anastomosis. This procedure was performed in 27 of the 40 cases with only 2 failures. In one of these the fistula occurred following a radical Wertheim hysterectomy for a Stage I carcinoma of the cervix following irradiation. As the other ureter was densely strictured, and the renal function was greatly impaired, a bilateral ureterovesical anastomosis was

done. The fistula recurred and the patient died of uremia 45 days after operation. In the other case an impassable stricture developed in the right ureter subsequent to operation at another hospital for right ovarian cyst and endometriosis. An attempted ureterovesical anastomosis could not be successfully accomplished, so the proximal ureter was ligated and nephrectomy subsequently performed.

Ureteroureteral anastomosis was performed only 3 times with only one success. In one of the failures, success was later achieved by ureterovesical anastomosis, while in the other, in which the ureter had been severed at the level of the infundibulopelvic ligament, nephrectomy was eventually per-

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TABLE IV. TREATMENT AND RESULTS

				8	UCCE	SS	F	AILUI	RE
	A	В	C	A	В	C	A	В	10
Ureterovesical anastomosis (1 previous unsuccessful ureteroureteral									
anastomosis)	11	7	8	11	6	7	0	1	1
Ureteroureteral anastomosis	3			1			2		
Repair of laceration over catheter	2			2			0		
No treatment (catheter perforation)	1			1					
Extraperitoneal drainage to									
catheter perforation	1			1					
Inlying catheter (1 laceration, 1 fistula)	1	1		1	1				
Nephrectomy (1 in Group A because of	-	-		_					
failure of ureteroureteral anastomosis)	1	2	2	1	2	2			
Ligation of proximal ureter (1 in Group A,									
hopeless ovarian carcinoma) (1 in Group									
C had subsequent nephrectomy)	1		1	1					1
Temporary nephrostomy with later treat-		3			3				
ment as follows:									
1 ureterovesical anastomosis									
2 (1 bilateral, 1 unilateral) incision of									
ureters above ligated areas and dila-									
tion from above plus inlying catheters									

Nephrectomy was necessary 5 times, in 2 for the reasons already mentioned, and in 2 others because the impairment of renal function on the involved side was so great as to render reconstructive operations useless. The fifth, a Spanish-American patient with a ureterovaginal fistula, would not remain for treatment, but returned to her home, where nephrectomy was

performed.

The group contains only 3 cases of unrecognized ureteral ligation, one bilateral and two unilateral. These were all successfully treated by temporary nephrostomy and later repair of the ureteral damage. In one of these with unilateral ligation, the damage was repaired by ureterovesical anastomosis. In the other 2, the dilated ureters were incised above the strictures resulting from the ligatures, and these strictures were dilated from above. After this, inlying catheters were placed up to the kidney and brought out through the bladder and urethra. They were left in place for an average of 10 days (Fig. 1). We feel that advocacy of this method of treatment for this unfortunate type of mishap cannot be too strongly emphasized. Some authorities, notably Herman, 6, 7, 8 have advocated immediate deligation as soon as the situation is recognized, but most of us familiar with the type of pelvic surgery in which such mishaps are likely to occur fully realize the technical difficulties to be encountered in such a procedure, and the hazards of a difficult surgical procedure in a patient as seriously ill as these patients usually are. A rather thorough review of the literature by Aschner⁵ has shown that in cases of bilateral ligation the mortality following immediate deligation has been between 80 and 90 per cent. Nephrostomy, on the other hand, is relatively easily accomplished,

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and the reconstructive procedures can then be more easily undertaken at a later date when the patient is in a generally improved condition, and the pelvic tissues have recovered from the trauma of the original operation.

The question frequently arises as to how long a kidney can withstand complete obstruction and still recover function. In one of our cases, recognition of a unilateral ligation with resulting nephrostomy did not occur until the eighteenth postoperative day, but function was recovered and reached an almost normal level (Fig. 2).



Fig. 1.—Intravenous pyelograms showing ultimate result in a case of bilateral occlusion of the ureters by ligatures placed on the ovarian vessels. Bilateral nephrostomy was performed as soon as the occlusion was recognized, and the injured ureters were repaired later. This film was made six months after the repair of the ureteral injuries.

Laceration or Incision of the Bladder Recognized and Repaired at the Time

There were 77 cases during the 21 years under consideration in which the bladder was inadvertently incised or lacerated, and in which the injury was recognized and repaired at the time. These cases have been divided into three groups:

A. Those in which the bladder injury occurred while the abdominal incision was being made, 15 cases.

B. Those in which the injury occurred during the course of the abdominal operation, for the most part while the bladder was being separated from pelvic or other abdominal viscera or masses, 48 cases.

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C. Those in which the injury occurred during vaginal operation, 14 cases.

In Table V may be seen the conditions for which the laparotomies were performed during which the bladder injuries in Groups A and B occurred. Again it will be seen that the predominating condition for which these laparotomies were performed was myomas of the uterus, but that in most instances this condition was complicated by an adhesion-producing condition, chiefly pelvic inflammatory disease.

The operations performed in Group A and the apparent reasons for injury to the bladder in this group are shown in Tables VI and VII. The opera-



Fig. 2.—Left retrograde pyelogram approximately two years after repair of a ligated left ureter. The ligation was not recognized until 18 days after its occurrence. Nephrostomy was then performed, and laparotomy with incision and dilatation of the strictured ureter from above gownward was carried out 24 days later. At the time this pyelogram was made phenolsulfonphthalein appeared from the left kidney in three minutes, and there was 20 per cent excretion from this kidney in a half hour.

tions performed in Group B, in which the bladder injury occurred during the course of the intra-abdominal operative procedure, are shown in Table VIII. The injury to the bladder was apparently due to its being densely adherent to the pelvic structures from which it had to be separated in the majority of these cases. In 4 cases the cause seemed to be the anterior position of a myomatous nodule. In 3 unusual cases, the injury occurred while the cervical stump was being suspended in one, during clamping of the uterine vessels in one, and while vaginal drains were being inserted in a case of unusually severe pelvic inflammatory disease.

The vaginal procedures during which perforation of the bladder occurred are shown in Table IX.

Twenty-nine of the operations in which these injuries occurred were performed by members of the visiting staff and the other 48 by members of the

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resident staff, which is probably very close to the ratio in which operations are performed on the service by these two groups.

Complications for the entire group were urinary tract infection in 14 and significant hematuria in 2. One patient died on the twenty-third post-operative day of pulmonary embolus, and another, the patient with sarcoma of the uterus, on the eighth postoperative day of uremia and cardiac failure.

The injury to the bladder in each case was recognized and repaired at the time of operation, and catheter drainage was instituted for an average of 10 days. No vesical fistula or other evidence of persistent injury to the bladder occurred in any case.

TABLE V. CONDITIONS FOR WHICH LAPAROTOMIES WERE PERFORMED DURING WHICH THE BLADDER INJURIES IN GROUPS A AND B OCCURRED

	Λ	В
Myomas of the uterus with pelvic inflammatory disease	7	21
Myomas of the uterus with adhesions from other causes		6
Myomas of the uterus with anterior nodule		4
Myomas of the uterus with ovarian cyst		1
Myomas of the uterus with sarcomatous degeneration		1
Pelvic inflammatory disease	3	4
Ovarian tumors (3 malignant)		7
Carcinoma of cervix, International Classification Stage 0		2
Carcinoma of cervical stump, International Classification, Stages I and III		2
Pseudohermaphroditism	2	
Full-term pregnancy	1	
Infected incisional hematoma	1	
Bilateral ruptured tubal pregnancy	1	
Total	15	48

TABLE VI. OPERATIONS DURING WHICH THE BLADDER WAS INCISED DURING THE ABDOMINAL INCISION, GROUP A

Hysterectomy, subtotal with unilateral or bilateral adnexectomy	8
Exploratory laparotomy (pseudohermaphrodites)	2
Bilateral adnexectomy	1
Total abdominal hysterectomy with left adnexectomy	1
Classical cesarean section	1
Excision of scar, repair of ventral hernia, and right adnexectomy	1
Drainage of incisional hematoma	1
Total	15

TABLE VII. APPARENT REASON FOR BLADDER INJURY DURING ABDOMINAL INCISION

Failure to catheterize preoperatively	2
Bladder adherent high to parietal peritoneum	5
Bladder unusually high on uterus (one cesarean section)	2
Incising incisional hematoma	1
Unexplained ·	5
Total	15

TABLE VIII. OPERATIONS DURING WHICH THE BLADDER WAS INCISED OR LACERATED DURING THE COURSE OF THE INTRA-ABDOMINAL PROCEDURE

Subtotal hysterectomy	7	
Subtotal hysterectomy with adnexectomy	25	
Total hysterectomy	2	
Total hysterectomy with adnexectomy	7	
Modified Wertheim hysterectomy	3	
Removal of cervical stump	2	
Attempted radical Wertheim on cervical stump	1	
Exploratory laparotomy	1	
Total	48	- 1

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TABLE IX. VAGINAL OPERATIONS DURING WHICH PERFORATION OF THE BLADDER OCCURRED

Watkins interposition operation	4	
Manchester type operation	3	
Vaginal hysterectomy	2	
Richardson composite operation	2	
Attempted removal of cervical stump Goebell-Stoeckel operation	1	
Construction of artificial vagina	1	
Total	14	

Vesicovaginal Fistula

During the same 21 year period, 56 vesicovaginal fistulas resulting from pelvic surgery were treated on our service. These will be discussed only briefly, as we intend to make these together with vesicovaginal fistulas from other causes the subject of another paper. Only 6 of these fistulas resulted from operations performed at the Johns Hopkins Hospital. In the other 50, the causative surgery had been performed elsewhere, and the patients came to us, usually after one or more attempts to close the fistula elsewhere. The types of operation resulting in the fistulas are shown in Table X. It is quite evident that the chief cause of these fistulas resulting from surgery is the operation of total abdominal hysterectomy. In view of our experience with recognized bladder injuries repaired at the time of operation, however, we do not believe that the fistulas result from incision or laceration at the time of operation, but rather from inclusion of a bit of the bladder wall within a suture during closure and peritonization of the vaginal vault. In one personal case, not included in this series because the fistula did not develop until after discharge, and the patient has never returned for repair, at the conclusion of the operation the patient was found to be bleeding vaginally from a small artery in the cuff. This could be controlled only by clamping, and it seems almost certain that a bit of bladder wall must have been included in the clamp.

TABLE X. OPERATIONS RESULTING IN VESICOVAGINAL FISTULAS

	J. H. H.	EL	SEWHERE
Total abdominal hysterectomy	4		37
Vaginal removal of cervical stump			7
Abdominal removal of cervical stump			1
Subtotal abdominal hysterectomy	1		
Goebell-Stoeckel operation	1		
Repair of cystocele			1
Excision of suburethral diverticulum			1
Cautery removal of vaginal cyst			1
Conization of cervix			1
Manchester operation			1

In the 56 cases, 80 previous attempts at closure had occurred before the final successful closure on our service. Eleven of these previous attempts had been made on our service, and 69 elsewhere. In the majority, there had been only one or two attempts, but in one case, there had been 8, in another 7, in 2 cases 4, and in 3 cases 3. It was a categorical rule of our preceptor in this line of work, Dr. Guy L. Hunner, that no attempt should be made to close a vesicovaginal fistula in less than six months from its inception or in less than six months following an unsuccessful attempt at closure. He felt that this length of time was necessary for the traumatized tissues to return to optimum condition for operation. We have found this a valuable rule to which to adhere, and most of those patients who have come to us following several

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unsuccessful attempts at closure have been subjected to these attempts in a matter of weeks rather than months. In such cases, both the patient and the surgeon are plagued by impatience, but here, as in most urological problems, patience is a virtue greatly to be commended. Dr. Conrad Collins has told us that the return of traumatized tissues to normal can be greatly hastened by the administration of cortisone, but as yet we have not had an opportunity to try this with regard to vesicovaginal fistula.

Forty-three of the 56 fistulas were successfully closed by the Latzko partial colpocleisis, in all but 2 on the first attempt, and in these 2 on the second attempt. This operation, introduced to American gynecologists by Holden⁹ in 1942, has been a tremendous asset in the management of this condition.

The other 13 were repaired by other vaginal methods with 2 failures. These were fistulas encountered before the introduction of the Latzko procedure, or those resulting from some other operation than a total hysterectomy, and hence too low on the vaginal wall to admit the Latzko technique. As evidence of the superiority of the Latzko procedure, there were 2 final failures in this group, and in 3 of those eventually closed there had been 2 previous unsuccessful attempts on our service. As this is considered an operation requiring the greatest possible experience, all but 2 were either performed or assisted in by a member of the visiting staff.

Comment

The incidence of urinary tract injuries here reported, we believe, is relatively small in consideration of the number of operations performed on the service during the same period of time, approximately 12,500 abdominal procedures, and 3,600 vaginal plastic operations including 500 vaginal hysterectomies. Including only those injuries resulting from surgery performed at the Johns Hopkins Hospital, 114 in all, this gives an incidence of approximately 0.7 per cent. Furthermore, the uniformly satisfactory results obtained in bladder injuries recognized and repaired at the time, and the initial success in all but 2 of the ureteral injuries recognized and repaired at the time indicate the importance of alertness in the recognition of this type of injury. Furthermore, the occurrence of only 6 vesicovaginal fistulas during the same period in which 77 bladder injuries were recognized and successfully repaired at the time of occurrence, we believe, speaks well for the alertness of our group regarding the possibility and essential hazards of urinary tract injury. We are quite willing to admit that we may be a bit biased in this regard, but we are inclined to attribute the small incidence of such injuries, and the large incidence of their recognition at the time of occurrence to the thorough training in urology and urological anatomy that all of our staff have experienced.

Our opinions as to the optimum methods of treatment for each type of injury have already been discussed and need not be repeated.

Conclusions

1. Urinary tract injuries resulting from pelvic surgery, while one of the most serious hazards of such surgery, need not occur frequently if careful attention is paid to the anatomy of the pelvic portions of the urinary tract.

2. If such injuries are encountered, recognition and repair at the time of occurrence give a better prognosis than later recognition and repair.

3. Serious injury to the ureter is best repaired by reanastomosis to the bladder where the injury is low enough in the ureter to make this procedure possible.

4. In the case of ureteral ligation unrecognized at the time, immediate deligation is to be condemned, and temporary nephrostomy with later repair of the ureteral defect highly recommended.

5. Bladder injuries recognized and repaired at the time rarely, if ever, lead to any serious difficulty.

6. Vesicovaginal fistulas resulting from total hysterectomy can usually be successfully repaired on the first attempt by use of the Latzko technique of partial colpocleisis.

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Discussion

DR. ALBERT H. ALDRIDGE, New York, N. Y. (By Invitation).-In this report, facts regarding 173 urinary tract injuries have been carefully summarized. About onethird of these injuries occurred at other hospitals and the patients were referred to the Johns Hopkins Hospital for treatment.

Of the 173 injuries reported, 77 (44.5 per cent) were bladder injuries. Conditions which led to these injuries were discussed and are well known to gynecologists. At times such injuries are difficult to avoid.

As a rule bladder injuries which occur during abdominal operations involve the dome of the bladder. They are usually recognized and can be safely repaired. Rarely do they complicate the postoperative course for any patient. The same may be said for most of the bladder injuries which occur during vaginal operations except for those which involve the urethra and neck of the bladder. In these locations injuries are more difficult to repair. Imperfect wound healing may lead to an occasional fistula or to stress incontinence of urine. In this series there were also seven vesicovaginal fistulas which resulted from removal of cervical stumps by the vaginal route. None of these occurred at Johns Hopkins.

The 40 ureteral injuries and ligations occurred during 6 radical operations for malignant disease; 33 abdominal operations for benign pelvic conditions, and one vaginal hysterectomy. For reasons stated we agree completely with the author's recommendation that ureteral ligations be treated primarily by nephrostomy rather than by immediate deligations. Nephrostomy is a much safer procedure for the patient and one which tends to preserve kidney function.

There were 56 vesicovaginal fistulas which followed 42 abdominal hysterectomies and 14 vaginal operations for benign pelvic conditions. Accidents occurring during complete abdominal or vaginal hysterectomy have been responsible for a high percentage of the vesicovaginal fistulas which have come under treatment in all clinics in the past few years. As a rule they are located in the vaginal vault and can be readily closed by the technique recommended by Latzko.

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Ten ureteral and bladder injuries resulted from radical operations for pelvic malignancy. In the most expert hands radical pelvic surgery is still accompanied by a 10 to 15 per cent incidence of serious urinary tract complications which to some extent defeat its benefits.

In reviewing such a series of surgical operations one can hardly fail to wonder how some of these accidents and injuries have been prevented. A striking feature of this report is the number of urinary tract injuries which occurred as a result of abdominal hysterectomies and removal of cervical stumps.

Accidents from subtotal or complete abdominal hysterectomies for benign pelvic conditions were responsible for about two-thirds (65 per cent) of the ureteral injuries, about two-thirds (65 per cent) of the bladder injuries, and three-fourths (75 per cent) of the vesico-vaginal fistulas. As pointed out by the author many of the hysterectomies were complicated by tumors beneath the bladder, intraligamentous tumors and cysts, pelvic inflammatory disease, and endometriosis.

Accidents during removal of the cervical stump by the abdominal route were responsible for one ureteral injury, 2 bladder injuries, and one vesicovaginal fistula. Technical risks of this procedure are obviously similar to those for complete abdominal hysterectomy.

In 1947, we reported on a technique for complete abdominal hysterectomy which has been in use at the Woman's Hospital since about 1940 and has been adopted by most of the members of our staff.

This technique permits ligation of the uterine blood vessels at about the same level as for the subtotal operation. The cervix is excised from the vaginal vault after it has been dissected free from the endopelvic fascial cuff which surrounds it and the cardinal ligaments have been clamped within the cuff and detached from the lateral surfaces of the cervix. By this technique there is no more risk of injury to the bladder and ureters than during a subtotal hysterectomy. Healing of the vaginal vault is promoted by careful hemostasis and a minimum of damage to the blood supply to structures in and about the vault. By this method we believe a cervical stump can also be safely removed by the abdominal route.

Since this technique was adopted two series totaling 1,500 consecutive complete abdominal hysterectomies have been reviewed. There were no known urinary tract complications in either of these series of operations, that is, no ureteral injuries or ligations and no postoperative ureteral or bladder fistulas. A considerable number of these hysterectomies were also complicated by intraligamentous tumors and cysts, and adhesion-producing adnexal conditions.

During both abdominal and vaginal operations we believe the risk of injuries to the urinary tract can be reduced by dissections in natural planes of cleavage and by keeping structures under moderate tension while dissections are being carried out.

Whenever possible we prefer to remove a cervical stump by the vaginal route. As a rule it is a relatively simple procedure and one which involves less risk of injury to the urinary tract.

We prefer to avoid the trauma of having catheters in the ureters during pelvic operations and are convinced that they are rarely needed to prevent injuries to the urinary tract.

DR. WALTER R. HOLMES, Atlanta, Ga.—While listening to his excellent paper I could not help thinking that Dr. Everett represents an outstanding example of what has become almost a lost species; a combination of gynecologist and well-trained urologist. His paper serves to emphasize the importance of this close association of the two specialities in the recognition, prevention, and treatment of complications of the female urinary tract. It seems to me that the members of this Association should encourage the younger gynecologists to take more interest in diseases of the female urinary tract in order that urology in the female may be returned to the domain of the gynecologist, where it rightfully belongs.

In looking over the records on my gynecological service at Emory University Hospital, 1933 to 1953, i.e., the years of Dr. Everett's study, I found there were 19 patients who had urinary tract injuries following pelvic operations. Of these there were 15 vesicovaginal fistulas and 4 ureterovaginal fistulas. Only 2 of the vesicovaginal fistulas in this series were the result of operations done at Emory University Hospital, both of these following radical

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hysterectomies for cancer. The remaining cases were referred following operations performed elsewhere. All of the operations in this latter group had been for benign lesions, i.e., hysterectomies for removal of fibromyomas.

The vesicovaginal fistulas in this group of private patients, 15 in number, were all successfully closed at the first attempt except in 2 instances which required 2 and 3 operations, respectively. The operations were all performed by the vaginal approach. All of the patients in this series, and I think this is very important, had a complete preoperative urological study. The methods used in closure of these fistulas were essentially on the principles first suggested by Marion Sims and modified by others; good exposure, careful mobilization of the bladder wall from the vaginal mucosa, closure of the fistulous tract without tension in two layers, fine catgut sutures in the bladder wall, and metallic sutures, silver wire or stainless steel, in the vaginal mucosa. Although this is a very small series, the good results obtained suggest that successful closure of these fistulas may be accomplished without use of the Latzko technique. My objection to partial colpocleisis is that it shortens the vagina and may result in marital difficulties.

I would like to emphasize one important point brought out by Dr. Everett. Surgical repair of these fistulas should not be attempted too soon after traumatic injury has occurred. A period of from four to six months as he has suggested should elapse before closure is attempted.

I also wish to congratulate Dr. Everett on his conservative and successful treatment of ureterovaginal fistulas. I must confess that my approach to this problem has been a more radical one. Where the other kidney showed normal function, a nephrectomy has been the operation of choice. I shall, in the future, try out the more conservative methods suggested by Dr. Everett in the treatment of ureterovaginal fistulas.

It is interesting to me to note that in Dr. Everett's series of cases, as well as my own, the vast majority of these urinary tract injuries occurred following operations performed outside the larger medical centers. This suggests to me that there may be something radically wrong with our surgical resident training program. Our large medical centers develop well-trained obstetricians and gynecologists but there are not enough of these well-trained specialists to go around and supply the needs of our smaller hospitals. There are in Georgia 73 recently constructed Hill-Burton Hospitals with a capacity of 3,769 beds. In the six states comprising the Southeast there are 252 recently-built Hill-Burton General Hospitals with a capacity of 14,374 hospital beds. These are well-equipped institutions and are staffed oftentimes with well-trained general surgeons, many of whom are certified in general surgery. The general surgeons in these hospitals, whether we like it or not, will continue to do hysterectomies.

Although I may be tried for high treason, I think our surgical residents during their hospital training should rotate through the gynecological service. The principles outlined by Richardson, Aldridge, and others make for a safe technique in performing total hysterectomy. It is a technique which is not too difficult to understand. At the same time, we may teach them when and why a hysterectomy should be done. It has been the policy on my service at Emory University Hospital for some time for the surgical resident to rotate for a time through the gynecological service. It is my firm belief that such a program, by giving these surgical residents a know-how in the technique of pelvic surgery, may be the means of preventing many of the urinary tract catastrophes, such as Dr. Everett has brought to our attention.

DR. JOHN PARKS, Washington, D. C.—Dr. Everett spoke of that important period after bladder injury until the time of surgical repair. He emphasized that if repair is not carried out immediately there should be a waiting recovery period of six months before surgery is attempted. The purpose in waiting is to allow as much spontaneous healing as possible to occur.

The report of a recent experience with a traumatic bladder injury may be helpful. When first seen two months after an automobile wreck, the patient had a suprapubic cystotomy tube and a fistula about 2 cm. in diameter in the bladder neck. The cystotomy tube was re-

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moved. A Foley catheter was placed in the fistulous tract until the cystotomy wound healed and until she developed bladder capacity again. This took about two weeks. The Foley catheter was removed from the fistula as soon as the urethra began to function again. To prevent seepage she used a vaginal tampon for a period of about ten days and began vaginal exercises. Surprisingly enough, she soon discarded the tampon procedure because it was possible for her voluntarily to prevent the loss of urine. This is the sixth week since she started voluntary exercises of the pubococcygeus and sphincter muscles. She can now go for two to three hours without losing urine although a fistulous tract about 1.5 cm. in size is still present. She has voluntary control of urine during the daytime, voiding a measured 200 to 250 ml. at a time. About the only time she has any incontinence is at night.

This illustrates that a fistulous tract through the sphincteric portion of the bladder neck can be partially controlled by voluntary muscular exercises during the natural healing period. After all induration and infection have subsided the fistula should be much smaller and much easier to repair.

DR. EVERETT (Closing).—There was one point that Dr. Aldridge made with regard to the technique of total hysterectomy with which we agree entirely. We do make an attempt to remove the cervix within the fascia, and that certainly minimizes the risk to the urinary tract. In some difficult procedures, particularly if the patient should go into shock, we do not always have the opportunity to do such careful dissection.

One of the cases included in our series illustrated this point. This was the patient in whom the left ureter was ligated and the ligation not discovered for 18 days. Hysterectomy was performed on the obstetrical service because of ruptured uterus at term. She was in severe shock, and there was a large hematoma in the right broad ligament. The intravenous pyelograms were done because the operator suspected injury of the right ureter, but it was the left one that was found to be ligated. Under such circumstances, it is not usually possible to dissect within pericervical fascia.

The total incidence of these injuries on our service, which I stated in the paper but did not read to conserve time, was extremely small, and most of the cases were very difficult.

The cases resulting from vaginal removal of the cervical stump, as we showed, did not occur on our service, but when there is such an injury, I believe it is because the bladder is adherent to the top of the stump above the fascia where the body of the uterus has been amputated. I frequently remove the cervix vaginally, and have not personally had an injury as result.

Dr. Holmes' experience with the Sims procedure apparently has been a little better than ours. Before 1940 we used the Sims procedure and this type of operation was usually done by Dr. Hunner who was an expert, if we ever had one, but his results were not as good as we have had with the Latzko technique. The operations often had to be repeated several times and there were 2 cases of final failure. The fistulas which follow total hysterectomy are usually very small, and the circle of mucosa that has to be denuded in the vaginal vault is not very large, so the procedure usually doesn't shorten the vagina more than 1 or 1.5 cm. at the most.

AN ANALYSIS OF 6,891 HYSTERECTOMIES FOR BENIGN PELVIC DISEASE*

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With Special Reference to the Safety of Routine Total Abdominal Hysterectomy

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WRITERS who cite the medical literature for their own purposes would do well to give heed to a number of facts. One of them is the date of the publication from which they are quoting. This precaution is particularly essential in gynecologic surgery. The face of this specialty has changed notably in the last two decades for a number of reasons, including the detailed attention now paid to preoperative and postoperative regimens, the liberal use of whole blood, the introduction of increasingly efficient antibiotics, and the establishment in hospitals all over the country of carefully supervised residency systems.

With full awareness of the risk against which we have just warned, we nonetheless elect to begin this discussion of total hysterectomy as a routine procedure with a quotation from a paper presented in 1932 by the late C. Jeff Miller, under whom I (C. G. J.) received my basic training in this specialty. Speaking of hysterectomy, the subject of the Hodgen Memorial Lecture, which he delivered in that year, he said:

It is perhaps the safest of the major abdominal procedures. It is perfectly standardized from the technical aspect. It is extraordinarily successful from the point of view of end-results But it is a successful operation only when it is performed upon the proper indications, a safe operation only when it is performed by properly qualified men.

Any discussion of hysterectomy should derive from those premises. This report, which urges the routine use of total hysterectomy in all cases in which abdominal hysterectomy is indicated, comes from the Department at the Tulane University of Louisiana School of Medicine which Dr. Miller once headed. We hope you will realize that in it the criteria of propriety and safety which he laid down for the performance of the operation are still strictly observed.

^{*}Presented at the Sixty-sixth Annual Meeting of the American Association of Obstetricians and Gynecologists, Hot Springs, Va., Sept. 8 to 10, 1955.

Historical Note

While it is not essential to this discussion, the past history of hysterectomy is sufficiently interesting to warrant a few words about it. Vigorous, sometimes acrid, debate over the merits of the total and subtotal operation has raged ever since the procedure was first introduced.² The first deliberate hysterectomy was performed in 1853 and for the next several years it was regarded, like McDowell's epoch-making ovariotomy, as outraging "fundamental principles of medical morality." Outstanding surgeons prayed to be delivered "from so much hysterectomy." Others, equally outstanding, regarded oophorectomy as a better method of managing uterine fibroids. As late as 1886 H. P. C. Wilson told the American Gynecological Society, "I shrink and have a feeling of terror come over me when I find myself obliged to do a hysterectomy."

As to the stump left in situ after the subtotal operation, it would be hard to think up anything that was not done with it. In 1892 Lusk thought that a recent suggestion for its management—now not worth the space to describe heralded "the dawn of a new day, when we could live at peace together, freed from this particular argument." It is probably true, as many writers have suggested, that the total operation, in spite of the risk involved when it was first introduced, was devised as the simplest way out of the dilemma of what to do with the cervix after the subtotal operation. Be this as it may, it is significant that Baldy, in 1894, while urging that the uterus be left in situ if even a portion of an ovary could be preserved, stated emphatically that it ought to be removed under all other circumstances, on the grounds (1) that it could make trouble after the adnexa were removed, (2) that these difficulties could not be corrected by extensive local treatment, and (3) that total removal of the uterus permanently eliminates the risk of future malignant disease. Sixty years later those are still sound arguments for the routine use of the total operation.

Evolution of Policies at the Tulane University School of Medicine

For the past quarter of a century there has been a clear-cut tendency all over the country, and particularly in teaching hospitals, to use total hysterectomy more often and subtotal hysterectomy much less often. In many institutions there has been a parallel tendency to increase the number of vaginal hysterectomies.

Both of these tendencies have been evident for many years in the Department of Gynecology of the Tulane University School of Medicine. At first the change in policy was no more than a trend. Then it became more and more pronounced. Finally, in 1950, Dr. Conrad G. Collins, Chairman of the Department, decided that subtotal hysterectomy would no longer be performed on the Tulane Gynecological Unit at Charity Hospital of Louisiana at New Orleans. Since rules are not always immediately enforceable, this particular rule was violated once in 1950 and once in 1951. Since Jan. 1, 1952, however, not a single subtotal hysterectomy has been performed on the

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Tulane Unit at Charity Hospital. During this period the uterus has been removed by either total abdominal or vaginal hysterectomy, according to the indications present in the individual case.

The trend to replace subtotal hysterectomy by the total operation became evident earlier, and has been even more impressive, in the private practices of the staff of the department. The experience of one of us (C. G. J.) is typical. In a private practice of sixteen and one-half years I have performed 639 hysterectomies for benign disease, only 9 of which, all performed before 1948, were done by the subtotal technique. Two hundred seventy of the remaining 630 operations were vaginal hysterectomies and 360 were total abdominal hysterectomies. There were no deaths in these 639 operations.

In short, in the private practices of the departmental staff, in which there is no compulsion, the total operation is now performed by choice almost as routinely as it is performed by departmental policy on the school service at Charity Hospital. The problems presented by extensive pelvic inflammatory disease on the school service are paralleled, to a lesser degree, by the problems presented by endometriosis in private practice. Yet in both private and public hospitals the policy of routine total hysterectomy whenever abdominal hysterectomy is indicated has proved as safe as it is practical. If it had not, there would be neither reason nor justification for continuing its routine use.



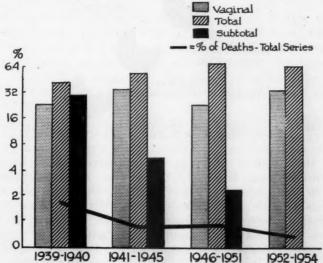


Fig. 1.—Mortality rate in relation to distribution of techniques in 6,280 hysterectomies (Table I).

Basic Data

Between 1939 and 1954, inclusive, 6,280 hysterectomies for benign pelvic disease were performed on the Tulane Gynecological Unit at Charity Hospital of Louisiana at New Orleans (Table I, Fig. 1). This material has been analyzed at intervals from 1941 through 1951. This contribution particularly concerns

the 1,246 hysterectomies performed in the 3 year period ending December 31, 1954, during which as already mentioned, no subtotal operations were performed.

TABLE I. DISTRIBUTION OF TECHNIQUES OF HYSTERECTOMY AND OF DEATHS ON TULANE GYNECOLOGICAL UNIT, CHARITY HOSPITAL, 1930-1954

	TOTAL SERIES		VAGINAL		TOTAL ABDOMINAL		SUBTOTAL	
PERIOD	CASES	DEATHS	CASES	DEATHS	CASES	DEATHS	CASES	DEATHS
1939-1940	828	14	199	2	374	5	255	7
1941-1945	1,768	13	659	2	997	11	112	0
1946-1951	2,438	19	657	2	1,669	11	112	6
1952-1954	1,246	5	436	0	810	5	0	0
1939-1954	6,280	51	1,951	6	3,850	32	479	13
Mortality rate	1	0.8	(0.3	(0.8	2	2.7

Before discussing these data and their implications, it might be well to state certain background facts about Charity Hospital of Louisiana at New Orleans. Exclusive of bassinets and of wards for such special services as the care of the premature infants, pediatric tuberculosis, contagious diseases, and



Fig. 2.—Racial distribution of admissions, gynecologic admissions, Tulane Unit admissions, and hysterectomies on Tulane service (Table II).

poliomyelitis, the hospital operates approximately 2,500 beds. Over the 3 year period ending June 30, 1955,* there were 202,346 admissions, of which 141,125 were to the Negro services (Table II, Fig. 2). No other hospital in the country has anything like this Negro population. Twenty years ago the hospital admissions were approximately 45:55 in favor of white patients. Over the years the balance has gradually shifted and the ratio is now 70:30 in favor of Negro patients. The disproportion is evident in the total gynecologic admissions, the admissions to the Tulane gynecologic unit, and the hysterectomies performed on the Tulane service. In all of these classifications the disproportion is of approximately the same order (Table II, Fig. 2).

Generally speaking, both the Negro and the white patients admitted to the New Orleans Charity Hospital represent the lowest level of financial incapacity. Negroes, even more than white patients in this stratum of society, are inclined to be careless of their health and indifferent to the laws of

^{*}Although the background hospital figures coincide with the period of the fiscal year, which ends in June, and the series of hysterectomies analyzed are based on statistics for calendar years, the discrepancy thus introduced is regarded as of no statistical or clinical significance.

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hygienic living and to the earliest signs of illness. As a rule, therefore, they present more advanced disease and more serious problems than are encountered in private practice.

Table II. Racial Distribution of Total Admissions, Gynecologic Admissions, and Tulane Unit Gynecologic Admissions and Hysterectomies, Charity Hospital, 1952-1955*

	WHITE	NEGRO	TOTAL
Hospital admissions	61,221	141,125	202,346
Gynecologic admissions	3,252	8,176	11,429
Tulane gynecologic admissions	1,279	2,823	4,102
Hysterectomies on Tulane Gynecological Unit	391	855	1,246

*See footnote p. 518.

Finally, this is a teaching hospital, and against the difficulties introduced by the conditions just described must be set the enormous advantage that in a teaching hospital residents, while they do a large proportion of the work, are carefully supervised and guided. Surgery in all branches is therefore kept within what has been well termed "the limits of surgical decency."

It is against this background that we are presenting the arguments for routine total hysterectomy in all cases in which abdominal hysterectomy is indicated.

An analysis of the hysterectomies performed over this 16 year period on the Tulane Gynecologic Unit at the New Orleans Charity Hospital shows two striking trends (Table I, Fig. 1). The first is the increasing tendency, even before the practice became official policy on the service, to perform total abdominal hysterectomy instead of the subtotal operation. The proportion increased from 45 per cent of all operations in the first period surveyed to 100 per cent in the last.

The second trend evident in these 6,280 hysterectomies is the steadily decreasing mortality rate (Table I, Fig. 1), which fell from 1.68 per cent in the first period surveyed to 0.4 per cent in the last. This progressive decrease would seem a convincing answer to the argument that the total operation is too hazardous to perform routinely, for the mortality rate continued to decline after the policy of routine total hysterectomy became absolute on the Tulane Unit at Charity Hospital.

When the 1,246 operations performed in the 1952-1954 period in which no subtotal hysterectomies were done are broken down (Table III), still another trend becomes evident—the increasing number of vaginal hysterectomies performed on Negro patients.

TABLE III. RACIAL AND YEARLY DISTRIBUTION OF HYSTERECTOMY TECHNIQUES AND DEATHS, CHARITY HOSPITAL, 1952-1954

TECHNIQUE	1952		1953		1954		ALL CASES	
	CASES	DEATHS	CASES	DEATHS	CASES	DEATHS	CASES	DEATHS
White.—					40			
Abdominal	55	0	55	0	40	0	150	0
Vaginal	75	0	78	0	88	0	241	0
All cases	130	0	133	0	128	0	391	0
Negro.—								
Abdominal	201	2	258	0	201	3	660	5
Vaginal	51	0	49	0	95	0	195	0
All cases	252	0	307	0	296	0	855	0
All Cases								
Abdominal	256	2	313	0	241	3	810	5
Vaginal	126	0	127	0	183	0	436	0
All cases	382	0	440	0	424	0	1,246	0

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year, es for inical Finally, one is struck by the wide age range in this series (Table IV, Fig. 3), particularly in Negro patients, 4 of whom were under 19 years of age, as well as by the safety of surgery in aging and elderly patients.

TABLE IV. AGE DISTRIBUTION IN 1,246 HYSTERECTOMIES, CHARITY HOSPITAL, 1952-1954

	ABDO	MINAL	VAGINAL		
AGE	WHITE	NEGRO	WHITE	NEGRO	
Under 19	0	4	0	0	
To 29	22	86	27	27	
To 39	52	277	67	81	
To 49	52	240	82	50	
To 59	20	40	41	20	
To 69	3	10	19	12	
70 and over	1	3	5	5	
Total	150	660	241	195	
Range	22-70	16-77	25-79	25-86	

HYSTERECTOMY:

DISTRIBUTION BY AGE AND RACE

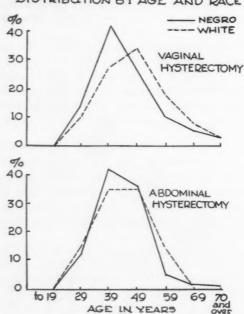


Fig. 3.—Age distribution in 1,246 hysterectomies (Table IV).

These various points will be considered in detail later in this paper. One other factor might be mentioned briefly at this time, that in our opinion the type of anesthesia employed for hysterectomy is not a matter of any importance, though the competence with which the anesthetic is administered is a matter of the gravest concern. Spinal analgesia was used in about two-thirds of the operations performed in the 1952-1954 period, and inhalation anesthesia was used in all but 7 of the remaining cases, all of which were vaginal hysterectomies performed under local analgesia for complete uterine prolapse in elderly women.

Indications for Hysterectomy

While the total operation is performed in all cases handled on the Tulane Unit at Charity Hospital in which removal of the uterus is indicated by the

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abdominal route, the decision to employ hysterectomy at all is always selective. As in most reported series (Table V, Figs. 4 and 5), fibroids furnished the most frequent indication. Just over a third of all the operations were for this cause, but the disparity in the distribution of cases between Negro and white patients is striking. Fibroids accounted for 31 per cent of all hysterectomies in Negro women, against 15 per cent in white women, and 88 per cent of the operations performed on this indication were in Negroes. These tumors, probably because of the patients' delay in seeking medical consultation, perhaps because of the natural course of the disease in this race, are larger, and more likely to be attended with complications, than they are in white women.

HYSTERECTOMY:

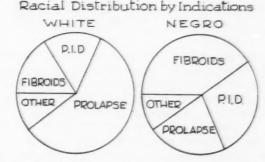


Fig. 4.—Racial distribution of indications for hysterectomy (Table V).

HYSTERECTOMY:

Racial Distribution of Indications

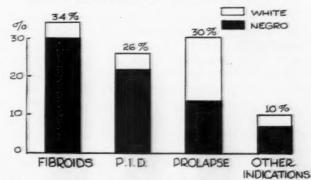


Fig. 5.-Racial distribution of indications for hysterectomy (Table V).

Pelvie inflammatory disease, including tuboovarian abscess, is regarded on the Tulane University Gynecological Service as a sound indication for total hysterectomy. Again the disparity between the races is striking. Eighty per cent of all operations for this indication were in Negro women, in whom, in our experience, the disease continues to be as frequent and as severe as it was before the antibiotics were introduced. This form of therapy, to be of any value, must be administered when the disease is in its earliest stage. Very few Negro women, and not many more white women of the social stratum treated at Charity Hospital, are seen at this period.

In the variety of pelvic inflammatory disease seen at this hospital, particularly in Negro women, both tubes and both ovaries are likely to be in-

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volved in the inflammatory process. Since they must be removed, the uterus, from the standpoint of function, becomes a useless organ, and an organ which is likely to be the origin of future symptoms. By our reasoning, it is much better out.

Table V. Distribution of Indications in 1,426 Hysterectomies, Charity Hospital, 1952-1954

			*
INDICATIONS	WHITE	NEGRO	TOTAL
Uterine fibroids	60	432	492
Pelvic inflammatory disease	58	308	366
Uterine prolapse, cervicitis	240	195	435
Tubal pregnancy	6	35	41
Postmenopausal bleeding	15	31	46
Endometriosis	9	13	22
Ovarian tumor	10	19	29
Total	398	1,033	1,431

Tuboovarian abscesses had developed in 116 of the 366 cases of pelvic inflammatory disease in this series, almost a third, and had gone on to rupture in 19 instances. The outlook in this catastrophe, which was formerly attended with a mortality rate of close to 90 per cent, has been reduced to between 15 and 20 per cent on the Tulane service at Charity Hospital by an aggressive surgical policy of immediate surgery, including, in a large proportion of cases, total abdominal hysterectomy. We have found that the removal of the uterus, whether the abscesses are ruptured or unruptured, is often more conservative, as well as considerably safer, than its retention. It is typical that 108 of the 116 tuboovarian abscesses in the series, and 17 of the 19 ruptured abscesses, occurred in Negro patients.

Total hysterectomy is also performed in both ruptured and unruptured tubal pregnancy, but only in carefully selected cases. The chief criterion of selection is that the patient must be in optimum condition, so that the additional procedure will introduce no additional risk. The reasoning, in the cases seen at Charity Hospital, is that the uterus is a useless organ after both tubes have been removed. It is significant that 35 of the 41 hysterectomies performed on this indication were in Negro women, who are particularly prone to present bilateral advanced pelvic inflammatory disease.

Like most modern gynecologists, we have broadened the indications for hysterectomy since it has become a procedure so free from risk. We now consider it both justified and indicated not only on such absolute indications as uterine fibroids but also, as has just been pointed out, in pelvic inflammatory disease, tubal pregnancy, and, indeed, any other condition in which pelvic surgery is indicated and in which childbearing is either no longer possible or would be impossible after the required surgery had been done.

This point of view perhaps needs some explanation and justification. Let me begin, therefore, by saying that we are entirely in sympathy with, and base our departmental policy on, the ethical principle that unnecessary surgery is never justified. But we do not regard surgery as unnecessary in a woman who continues to have symptoms after a fair trial of nonsurgical treatment if in our opinion she can be relieved of her symptoms, and restored to health and usefulness, by the removal of an organ that is no longer useful. We take the position that the principal function of the uterus is childbearing. Once childbearing has become impossible, whether by reason of age or by the development of a pathologic process, the uterus becomes a useless organ. Menstruation is not necessary, either physiologically or psychologically, to a

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woman's health and well-being. There is therefore no virtue in its preservation per se, and even less virtue in its maintenance after it has become a perverted function.

For these reasons we question some of the surveys, in both the medical and the lay press, concerning what is termed the abuse of hysterectomy. Certainly the operation has sometimes been employed without justification, though chiefly, we think, by operators who are not trained gynecologic surgeons. There is also no doubt that it is sometimes performed on less than the soundest indications and on less than the best motives. Our staff, however, also takes the position, and in it we have much good company, that it takes more than the examination of a hospital chart and the review of a pathologic report, even when the report is negative or equivocal, to tell the whole story of why an operation was performed and why a surgeon elected to follow a certain course in a certain case. That is a judgment which can be arrived at only by a study of the patient herself, not simply by a review of her hospital records.

Previous Conservative Surgery.—One reason for the stand that we have taken in regard to total hysterectomy is our increasing doubt as to the wisdom of conservative treatment in certain pelvic diseases. An examination of the literature from this standpoint shows why the belief is growing that conservative treatment in itself is not necessarily desirable and that it may, in fact, end by being anything but conservative. When a patient who comes to hysterectomy has undergone previous pelvic surgery in which the uterus was retained, the reasonable assumption is that the previous operation was performed on the laudable—though frequently fallacious—ground that preservation of tissue is always better than extirpation of tissue. This is not necessarily true. The argument against such a policy would be even stronger if all so-called conservative operations were followed up, but even the incomplete evidence is extremely convincing.

Sixty-seven of the 810 patients submitted to total abdominal hysterectomy and 40 of the 436 submitted to vaginal hysterectomy in the 1952-1954 series at Charity Hospital had previously undergone surgery of the so-called conservative type (Table VI). Some of these operations were performed from 10 to 30 years before hysterectomy was required. Some of them were undoubtedly justified when they were performed, partly because of the pathologic processes present and partly because of the practices current at that time, but these extenuating circumstances do not explain away two facts: the first is that in 25 of the 117 patients who later required abdominal or vaginal hysterectomy the primary procedure had been such that pregnancy was no longer possible and the patient was left with a useless organ from the standpoint of the childbearing function. The second fact is that many, if not most, of the primary operations failed to relieve the symptoms for which they were performed, and that in a certain number of instances the operations which had been performed were directly responsible for the development of other symptoms.

This list, it should be noted, concerns only previous surgery. Not included are a number of cases in which radium or x-ray had been employed for functional bleeding. This is a method which has not been used on this indication on the Tulane service for about 20 years. The results are highly uncertain, aside from the disadvantage that irradiation offers no protection against the later development of cervical or endometrial carcinoma.

Our own experiences concerning the need for hysterectomy after conservative surgery are borne out by the literature. Burch and Lavely,3 for

instance, reported that previous surgery had been performed in 26 per cent of their 1,221 hysterectomies. In their opinion the second operation was often directly necessitated by the first. Leventhal and Lazarus,⁴ Phaneuf,⁵ Tyrone,⁶ and others have made similar reports.

TABLE VI. PREVIOUS OPERATIONS IN 117 PATIENTS LATER SUBMITTED TO HYSTERECTOMY

OPERATION	CASES	YEARS EARLIER	
Plastic	11	1-18	
1 plastic on cervix also			
2 amputation of cervix also			
Suspension of uterus	12	4-24	
Tubal ligation	17	1-16	
3 suspensions of uterus also			
2 oophorectomy also			
Salpingectomy, unilateral	19	1-12	
Salpingectomy, bilateral	2	6-47	
Salpingo-oophorectomy, unilateral	22	1-30	
1 in 2 procedures			
1 uterine suspension also			
Salpingo-oophorectomy, bilateral	4	6-19	
Salpingectomy, bilateral, oophorectomy	4 2	6	
Oophorectomy, unilateral	15	3-13	
Oophorectomy, bilateral	1	12	
Resection of ovary	2 9	1-7	
Myomectomy	9	2-10	
1 unilateral oophorectomy also			
1 unilateral salpingo-oophorectomy also			
Ligation vena cava	1	6	

Tyrone's careful breakdown of 810 previous operations in a series of 2,334 hysterectomies performed over a 21 year period is particularly striking. Not a single woman submitted to previous conservative surgery became pregnant after it. This might have been expected, for the earlier operations included 220 bilateral salpingectomies, a procedure which eliminates immediately any possibility of pregnancy. Three hundred seventeen of the 810 women were over 40 years of age, and 94 were over 50, when the first operation was done. Pregnancy is infrequent in the fifth decade and practically unheard of in the sixth. Of the 41 patients who underwent myomectomy, only 1 was under 30 years of age, the most favorable period for conception, at the time the operation was performed. One hundred seventy of the previous operations were suspensions of the uterus, a procedure now recognized as practically without value. Finally, not a single one of these 810 women was relieved of her symptoms by the previous operation, and all of them eventually had to undergo the hysterectomy from which, undoubtedly with the best of motives, they had been protected at the first operation.

In the light of these facts, we feel that our position that hysterectomy should replace so-called conservative surgery in a large majority of all cases is based on sound reasoning and is in the patient's best interests. If the gynecologist takes the position, as he most certainly should, that his objective is to relieve the patient of symptoms, then hysterectomy is fully justified if pelvic surgery is required in women in whom childbearing is no longer a consideration. Furthermore, since this operation, as our figures show, has become so safe, there is every reason why it should replace, in the vast majority of instances, such formerly popular procedures as the Manchester operation, Watkins' interposition operation, uterine suspension, and various plastic procedures on the cervix.

The Case for Routine Total Hysterectomy

The case for routine total hysterectomy in all instances in which abdominal hysterectomy is indicated is based on a number of sound arguments:

Persistence of Symptoms after Subtotal Hysterectomy.—The most obvious reason, perhaps, for performing total instead of subtotal hysterectomy as a routine is the number of extremely annoying symptoms which may follow the retention of the cervix. Among them are persistent spotting or frank bleeding; cervical infections, including cyst formation, bilateral pelvic pain and low back ache, dyspareunia, and prolapse of the cervix.

One of the best arguments, albeit an unconscious one, for the routine use of the total operation is provided by advocates of the subtotal operation who, at the time the incomplete operation is done, perform a variety of procedures on the cervix, ranging from conization and cauterization to amputation by the Sturmdorf or some other technique. Aside from the well-established fact that the morbidity of the supracervical operation is likely to be increased by preliminary procedures on the cervix, especially conization, the argument is simply not sound that adjunct surgery on the cervix produces as good end results as removal of the uterine corpus and cervix en masse. If the cervix is sufficiently diseased to require surgery, it is far more logical to remove it along with the body of the uterus. It is unhealthy in a large proportion of the cases in which hysterectomy is indicated. Wallace,7 reporting 153 total hysterectomies performed in private practice, noted that in 83 per cent of the cases the cervix was sufficiently diseased to be included under separate diagnostic headings in the pathologist's reports. His experience is not unique.

Carcinoma of the Cervical Stump.—The most impelling argument in favor of total as compared with subtotal hysterectomy has always been that total removal of the uterus eliminates forever the risk of development of carcinoma of the cervix. This is an irrefutable argument. It always was irrefutable, but there was something to be said against it in the days when the mortality rate of total hysterectomy materially exceeded the risk of the development of cancer in the cervical stump.

In 1955 this argument no longer holds, though there are, unfortunately, no trustworthy figures on the incidence of carcinoma of the cervical stump. In 1945 in a follow-up study of 500 carcinomas of the cervix treated at least 5 years earlier at the New Orleans Charity Hospital, Graffagnino⁸ found 27 instances of carcinoma of the cervical stump, 5.4 per cent. For the years 1941-1947 inclusive there were 68 cancers of the stump at this institution in a total of 943 cases of cervical cancer, an incidence of 7 per cent, which is close to the incidence of 7.3 per cent reported by Dodds and Latour in 1997 cases of cervical cancer at the Royal Victoria Hospital in Montreal and by Stearns in 1953 from the University of Oregon.

Randall and Gerhardt,¹² on the basis of statistics collected in New York, where cancer has been a reportable disease for many years, estimate that at the present time nearly 4 per cent of all women over 20 years of age are likely to develop a malignancy of the uterus (2.28 per cent of the cervix and 1.55 per cent of the corpus). To argue the case for total hysterectomy from a sound statistical basis, however, it would be necessary to have precise follow-up figures for all the subtotal hysterectomies done in a particular institution or by a particular surgeon. Very few such series exist, but it is significant that when they are available, the observers who have collected them are strong advocates of total hysterectomy. Donnelly and Bauld, ¹³ for instance, who found an incidence of 1.58 per cent for carcinoma of the cervical stump

in 2,623 supracervical hysterectomies and a mortality rate of 0.81 per cent in 1,077 total hysterectomies, now regard the total operation as mandatory. In this connection, it might be pointed out that the passage of years offers no protection against the development of malignancy of the stump; in one of the cases reported by Stein,¹⁴ for instance, the malignancy developed 26 years

after the original operation.

Even surgeons who are still performing subtotal operations in some cases practically always agree that cancer of the stump is a possible future risk, and also agree that this is a risk which now outweighs the risk of death after the total operation. Certainly on our own service, on which the mortality rate of total abdominal hysterectomy has been a fraction of 1 per cent for a number of years, the risk of this operation is now very considerably less than the risk of the development of cancer of the cervical stump and of death from that disease. The argument occasionally advanced that the malignant disease does not usually develop in the retained cervix but in most cases is present at the original operation is a half-truth which makes little difference to the patient who has the disease and is, in fact, a disturbingly lighthearted way of meeting a serious challenge.

Total Abdominal Versus Vaginal Hysterectomy.—While we have eliminated subtotal hysterectomy from our gynecologic procedures, that does not mean that we employ the total abdominal operation except by deliberate choice. We have found vaginal hysterectomy an increasingly useful operation (Tables I and III, Fig. 1). This technique has always been popular on the Tulane Service at Charity Hospital where it was employed by Dr. C. Jeff Miller at a time when a great many gynecologic surgeons did not look upon it with particular favor. For the most part, however, he limited it to cases of uterine prolapse, and for this reason he did not perform it very often in Negro women, in whom this condition was, as it still is, far less common than in white women. We are now using vaginal hysterectomy with increasing frequency in our Negro patients, although still much less often than in white women. This is chiefly because the vaginal operation is contraindicated in uteri fixed by adhesions from pelvic inflammatory disease, as well as in large fibroids which could be removed vaginally only by morcellation. We regard the vaginal technique as of special value in elderly women, obese women, and women who are poor surgical risks, regardless of race.

We do not feel that abdominal hysterectomy and vaginal hysterectomy are in any way competitive. We regard them as complementary procedures. Each of them has its own independent field of usefulness. In short, we belong to the large group of gynecologic surgeons described by Leventhal and Lazarus⁴ as employing both the vaginal and the abdominal technique "with

equanimity."

The Safety of Routine Total Hysterectomy

In the past, one of the chief arguments for the subtotal operation has been that it was a safer procedure for the less experienced surgeon, particularly the general surgeon and the occasional operator. Whether the inexperienced surgeon and the occasional operator should be performing hysterectomy at all is not a part of this discussion, but certainly the argument that the subtotal operation is safer than the total operation is no longer valid. It is still true, however, that the citation of mortality rates requires a knowledge of their origin. In this connection, Miller, in the Hodgen lecture, quoted Black to the effect that the mortality rate for the complete operation in unselected cases was 8 to 9 per cent, and that in every 100 total hysterectomies in which the experienced surgeon would lose 1 life his less skilled confrere would lose 4.

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This is almost 25 years later. Mortality rates of 8 to 9 per cent for any type of hysterectomy would not now be tolerated in any hospital. The rate for total hysterectomy in our last series at Charity Hospital was 0.5 per cent. I (C. G. J.) have never had a death as a result of this operation in my private practice. A review of the recent literature shows comparable results in many collected series, though the statistics are difficult to present as tabular data because the methods of analysis vary from series to series. The safety of the operation is thus the chief argument for routine total hysterectomy. When the low mortality rate is combined with the relief of symptoms referable to the uterus and cervix, and with absolute protection from future malignancy of the cervix, there seems little reason for continuing to perform an operation which is attended with at least equal risk, and which is also attended with the chance of persistence of symptoms referable to the cervix and with the possibility of future malignant disease.

Various other arguments against total hysterectomy and in favor of the subtotal operation need no extended discussion. In our experience, the total operation takes very little more time than the subtotal. The loss of blood should be no greater in the total operation. The hazards to bladder and ureter, of which the advocates of the subtotal operation make so much, are entirely avoidable. In short, we regard it as quite possible, as Stearns¹¹ puts it, to keep the total operation both safe and feasible by attention to such details as avoidance of mass clamping and mass ligature; precautions to protect the ureters and bladder; and precautions to maintain the normal vaginal depth, preserve the pelvic supports, and conserve the blood supply of the ovaries when they are retained.

If we were achieving our good results with total hysterectomy only by selection of cases, our advocacy of the routine use of this technique would be on a very unsure basis. We do not select our cases. When the proper indications for hysterectomy exist, we perform the total operation just as readily on poor surgical risks as on good risks. No patient is ever refused surgery for medical reasons. We therefore cannot accept seriously the argument that the subtotal operation is less hazardous in cardiac subjects, hypertensive, tuberculous, or diabetic patients, and others with organic disease.

In these 1,246 cases 244 patients had hypertension (160/110 mm. Hg or over), or cardiac disease confirmed by electrocardiography, or both. Twentynine patients had diabetes. Nine had pulmonary disease, chiefly tuberculosis and bronchiectasis. Five had frank renal disease. In addition, there were 9 instances of mental disease, chiefly schizophrenia. Only 1 of the 5 deaths, as will be pointed out later, occurred in a patient with organic disease, and there seems no reason to believe that the use of the subtotal technique would have altered the outcome in that case, for the complete operation was performed with no difficulty whatsoever.

It should be emphasized, of course, that while we do not refuse surgery to any patient with organic disease in whom hysterectomy is indicated, we are most careful to see that all complicating disease is completely under control before operation is undertaken. This means close cooperation with a competent internist both before and after operation. We fully agree with the aphorism that surgery in such cases is safe only because the patient is regarded as unsafe and in need of careful, dual supervision throughout her course.

Postoperative Morbidity and Complications.—The postoperative morbidity in this series, using the standard of a temperature elevation to 100.4° F. on any 2 consecutive days or of 102° F. on any single day, was 48 per cent in

the 810 abdominal operations and 53.4 per cent in the 436 vaginal operations. In the great majority of cases the temperature elevations were transient and of no consequence.

Most of the postoperative complications (Table VII) were also transient and inconsequential. The incidence in the 810 abdominal operations was 17.4 per cent and in the 436 vaginal operations 24.8 per cent. Urinary tract complications predominated. As to the remainder, most of them are quite as likely to occur after the subtotal as after the total operation. Hematomas and abscesses of the vaginal cuff, which occurred in 14.6 per cent of the total operations, cleared up promptly in every instance. Only 1 of the 4 fistulas, a ureterovaginal fistula, required subsequent surgery (nephrectomy).

TABLE VII. POSTOPERATIVE COMPLICATIONS IN 1,246 HYSTERECTOMIES, 1952-1954

COMPLICATION	ABDOMINAL	VAGINAL	TOTAL	
Urinary	141	108	249	
Hematoma, vaginal cuff	34	44	78	
Abscess, vaginal cuff	7	33	40	
Infection (disruption), abdominal wound	15	0	15	
Hematoma, abdominal wound	11	0	11	
Intra-abdominal hemorrhage	2	5	7	
Intestinal obstruction	3	0	3	
Homologous serum jaundice	1	0	1	
Reaction transfusion, infusion	9	3	12	
Vascular complications:				
Pelvic thrombophlebitis	3	0	3	
Cerebrovascular accident	0	1	1	
Pulmonary embolism	2	0	2	
Atelectasis	4	1	5	
Pneumonia	2	3	5	
Fistula:				
Rectovaginal	2	0	2	
Vesicovaginal	1	0	1	
Ureterovaginal	1	0	1	

Role of Resident-Training.—These results, which are good by any standard, were not accomplished by mere chance. On the Tulane University service at Charity Hospital the bulk of the surgery is done by residents in training, but by residents who are supervised with the greatest care. First year residents do no surgery at all. Second year residents operate under supervision. Third year residents are permitted to operate independently, but members of the visiting staff are present for all operations in which any difficulty might be expected, including all instances of large fibroids and all cases of extensive pelvic infection. The visiting staff performed only 83 of the 1,246 hysterectomies recorded for the 1952-1954 period. All 5 deaths occurred in operations performed by residents, but in 2 of the 5 cases members of the visiting staff were present.

Another point to be emphasized in this connection is the sound training which all residents receive in the preoperative and postoperative management of gynecologic patients. Surgery, it is taught, is only one phase of gynecologic care. The excellent results which we are achieving are attributable, in large measure, to the fact that total management of the case, and not its surgical management alone, is constantly stressed.

On the other hand, residents are also soundly trained in surgical technique, though for the last 5 years they have been taught only the total abdominal and vaginal techniques of hysterectomy. Since they are trained, both by teaching and by example, only in these techniques, it does not occur to them that the complete operation cannot be performed routinely where an abdominal hysterectomy is indicated. The fractional mortality achieved by this training policy is our justification for continuing to employ it.

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Fatal Cases

The 5 deaths which occurred in these 1,246 hysterectomies all occurred in total abdominal hysterectomies and all in Negro women.

Case 1.—A 56-year-old Negro woman, admitted Sept. 11, 1952, with a complaint of abdominal pain, was thought to have degenerating uterine fibroids and pelvic peritonitis. Her course was septic, and foul-smelling pus was obtained by aspiration of the cul-de-sac. Laparotomy, performed after 9 days of conservative management, revealed a left tubo-ovarian abscess, with edema and thickening of all the pelvic structures, including the uterus. Total abdominal hysterecomy and bilateral salpingo-oophorectomy were performed with some difficulty.

The immediate postoperative course was stormy. Ileus was controlled by the use of the Miller-Abbott tube. Under cortisone and Sulfathalidine therapy the patient became afebrile and the rectovaginal fistula which had developed after operation apparently closed, though a large mass which was present anterior to the rectum continued to be felt. Twenty-four days after operation the patient suddenly went into shock and the mass could no longer be felt. The abdomen was extremely rigid and no peristalsis could be heard. Exploration revealed no evidence of peritonitis and the abdomen was closed without further exploration. Ten days after the second operation feces again drained from the vagina, apparently from another large mass anterior to the rectum. Shortly after this examination the patient went into shock and death occurred a few hours later.

Autopsy disclosed an annular carcinoma of the sigmoid colon, 15 cm. from the anus. The tumor had eroded into the vaginal cuff, producing a colovaginal fistula and peritonitis.

In this case, as is obvious, the primary diagnosis was missed, partly because all the symptoms pointed to the pelvis and partly because exploration would not have been justified at the first operation in view of the suppurative pelvic process. Whether the patient would have lived longer if a subtotal instead of a total operation had been performed is an academic question. The technique employed apparently had nothing to do with her death.

CASE 2.—A 30-year-old Negro woman, admitted to the hospital Nov. 13, 1952, with abdominal pain of 3 months' duration, had been treated earlier, on another service, by colpotomy, with drainage of 350 c.c. of purulent exudate from a cul-de-sac abscess. The day after admission she suddenly went into shock, and immediate laparotomy confirmed the diagnosis of rupture of a tuboovarian abscess; the peritoneal cavity contained 700 c.c. of purulent material. The uterus and cervix, tubes and ovaries were removed. Feces were passed by vagina November 21, and 3 days later the abdominal incision ruptured in the upper third. The blood pressure remained at shock level after secondary closure of the wound and death occurred suddenly 3 days later. The urea nitrogen had gradually risen after the second operation and was 80 mg. per cent just before death.

Autopsy revealed pelvic peritonitis, a rectovaginal fistula, multiple renal abscesses, pyelonephritis, and acute bacterial endocarditis.

In this case total hysterectomy was performed without difficulty and death is attributable to septicemia from the original pathologic process rather than to the technique of hysterectomy.

CASE 3.—A 53-year-old Negro woman, admitted Feb. 15, 1954, with the diagnosis of degenerating uterine fibroids and pelvic inflammatory disease, was found at laparotomy February 20 to have a right tuboovarian abscess as well as fibroids. Total abdominal hysterectomy was performed, with bilateral salpingo-oophorectomy. The following day she went into sudden shock and the abdomen was immediately reopened. There was no evidence of the intra-abdominal bleeding which had been suspected. During the operation the blood pressure rose to 170/90 mm. Hg. The medical consultant who had supervised the preparation of the patient for operation because of hypertensive cardiovascular disease expressed the opinion that the shock episode had been caused by the Adams-Stokes syndrome. Ileus, which

developed February 25, was controlled by the Miller-Abbott tube. Symptoms and signs of mechanical intestinal obstruction appeared March 5, but exploration was negative. Death occurred 2 days later.

The urea nitrogen of the blood rose progressively after the first operation, reaching 77 mg. per cent March 3. An electrocardiogram on this date showed Wenckebach's phenomenon.

Autopsy was not permitted in this case but the cause of death was obviously renal failure, superimposed on the original hypertensive cardiovascular disease. A member of the staff was present at the first operation and was in consultation throughout the post-operative period. The internist called in consultation as soon as the patient entered the hospital cleared the case for surgery and supervised the post-operative course. This is the only death which occurred in the 296 patients with organic disease, and, since operation was performed without difficulty, it seems unlikely that the technique employed had anything to do with the outcome.

Case 4.—A 42-year-old Negro woman, admitted May 25, 1954, with a complaint of severe epigastric pain and vomiting for 24 hours, was sent to a surgical service, where she was treated conservatively for a week with the diagnosis of acute pancreatitis. Exploratory operation on June 2 revealed a partial intestinal obstruction, caused by pelvic adhesions, and a cystic mass involving the right adnexa. The gynecologic resident who was called into the case at this point removed the tube and ovary with considerable difficulty and then performed total hysterectomy as the simplest way of controlling massive bleeding from the right uterine artery. While the cervix was being freed, the sigmoid was accidentally opened. It was closed without difficulty and a transverse colostomy was performed.

Although the patient received 8 units of blood during the operation and the blood pressure at the conclusion was 100/70 mm. Hg, it fell to shock level shortly afterward and death occurred 20 hours after operation; there was no response to intensive therapy. Urinary output after operation amounted to only a few drops.

Autopsy was not permitted in this case, but the death must be regarded as preventable and due to technical errors at operation.

CASE 5.—A 53-year-old Negro woman underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy Nov. 1, 1954, for a very large uterine fibroid and a tubo-ovarian abscess. Secondary closure of the wound was necessary on the eighth day for a wound separation extending down to the fascia. Death occurred suddenly 12 hours later, and autopsy revealed an embolism involving the left pulmonary artery at the bifurcation. The technique of hysterectomy employed is not regarded as having influenced the fatal outcome.

Summary

1. For many years hysterectomy has been the safest of all major abdominal procedures and has been extraordinarily successful from the point of view of end results.

2. For these reasons the indications for the operation have generally been extended, and it is now regarded as the preferable procedure whenever pelvic surgery is required in women in whom childbearing is no longer possible or in whom it would be impossible after the necessary pelvic surgery had been performed.

3. This point of view has for many years been accepted in the Department of Gynecology of the Tulane University School of Medicine, which also, since 1950, has followed the policy of performing total hysterectomy routinely when the abdominal operation is indicated. This rule has not been violated since 1951. As the subtotal operation decreased in popularity, even before this policy went into effect, the vaginal technique was employed more frequently, particularly in Negro women.

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- 4. The policy of routine abdominal hysterectomy is justified by the end results, which include the elimination of symptoms referable to the retained cervix and the elimination of the possible development of cancer of the cervical stump. The policy is also completely justified by the safety of routine total abdominal hysterectomy.
- 5. The good results achieved by this policy are attributable to a variety of Chief among them are the practice of medical consultation in all cases of associated organic disease and the careful supervision of residents in training, who do the bulk of all gynecologic surgery.
- 6. This contribution is based upon an analysis of the 6,280 hysterectomies performed on the Tulane Gynecological Unit of Charity Hospital of Louisiana at New Orleans between 1939 and 1954, inclusive, and in particular upon the 1,246 operations performed in the 1952-1954 period, when the policy was in effect of performing routine total abdominal hysterectomy whenever abdominal hysterectomy was indicated. The mortality rate for the whole period was 0.8 per cent and for the 1952-1954 period 0.4 per cent. A series of 639 hysterectomies performed in private practice over a sixteen and one-half year period is also briefly discussed from the standpoint of the safety of routine total abdominal hysterectomy.

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Discussion

DR. FREDERICK S. WETHERELL, Syracuse, N. Y.—The urge which prompted Dr. Johnson to restate the idea that supravaginal hysterectomy has no place in gynecologic surgery is evidence, sadly enough, that the teaching of many members of this Association, notably our beloved John O. Polak, has been missing its mark even at this late date. Polak's repeated admonishments, more than 35 years ago, regarding the world-wide incidence of malignancy in the retained cervical stump, prompted at least a few of us to discontinue completely the supravaginal operation.

My first panhysterectomy was done in 1921. Those were the days when all too often you could not see the uterus for the clamp handles sticking up in all directions. Even today you can see this sort of thing despite the fact that another of our members, William Weir, showed us at our mid-year clinic in Cleveland, in 1930, that hemostats were only an encumbrance, that only two were needed alongside the uterus for traction. That technique greatly simplified the operation of total hysterectomy. From that day on I added another admonishing voice which, at least in Central New York, was truly a voice in a wilderness of pelvic hemostats.

My representations were not well taken by my "supravaginal ectomist" colleagues. "Too much danger of a prolapsed vaginal vault," they said. "Removing a vaginal cuff with the cervix will shorten the vagina," they added. Please note that the authors also speak about avoiding shortening the vagina. Do we forget the age-old technique that can readily lengthen such an easily dilatable organ? Let us forget this untenable argument against panhysterectomy.

From personal observation I can say that lack of surgical acumen and good judgment, as well as a hurry to get at it, is the outstanding reason for the numerous supravaginal hysterectomies we had in the past, and the few that are still being done. Add to this the other rationalizations, such as obesity, to mention one, and we can understand why, when arguments came from assumedly high places, many of the lesser lights took what they felt was the easier way. With these preliminary remarks in a vein which my older colleagues of this Association expect me to display, in keeping with past performances, I will tell you how the pressure on Central New York State recalcitrants has worked.

Aaron B. Miller, a Founder of this Association, my Chief and preceptor from 1914 to 1921, and Professor of Gynecology at Syracuse University, College of Medicine, occasionally did a panhysterectomy. When Polak published his findings Dr. Miller agreed with them. He agreed, too, that I should begin doing the total operation only. He backed me faithfully against the contentions of his successors in the department, and one or two general surgeons, that it might be well enough for Polak to do such a formidable operation but that I was going a bit too far.

This "battle" continued into the 1940's until, in 1948, a resident reviewed the cases of supravaginal hysterectomy done in the teaching hospital by the teaching group. His research disclosed the fact that malignancy developed in over 2 per cent of the retained stumps. The latest survey shows that 2 carcinomas of the retained stump were found in 1950, in cases where the original operation had been done in 1944. Shortly after that time a new regime took over and began to do routine total operations. Even so, the records show that, from the years 1950 through 1953, 4 supravaginal hysterectomies were done in that teaching hospital, 3 of them by two general surgeons, and one by a former member of the gynecologic staff. In 4 hospitals in Syracuse, in which it is possible to exercise a certain degree of control, there were 11 subtotal operations done. None were done in 1954 and none so far in 1955. To me it has seemed like a Forty Years' War, which in truth it just about has been.

The authors infer, in their introductory paragraph, that poor preoperative and postoperative care, and lack of blood transfusions and antibiotics, made the operation of
panhysterectomy a dangerous one in the past. That danger being no longer existent, the
argument for supravaginal hysterectomy, should be eliminated. The authors quote Jeff
Miller as saying that (1) the operation is the safest abdominal one; (2) the technique
is standardized; (3) it is extraordinarily successful as to end results; (4) but (the big
"but" which still holds true) it must be performed by properly qualified men. This was
said in 1932. Our self-policing methods have been terribly slow but have now come to a
point where it is no longer necessary to consider the suggestion of some recent lay writers
that disciplinary legislation should be adopted.

Good gynecologic surgeons of the "past" perhaps did not need as much in the way of blood and antibiotics. Blood has of course been available since 1919, even before that. But, back there, the good surgeon moved along; he did not waste time for two or more hours; he did not take 15 minutes to enter the peritoneum. Such loss of time can often be seen in this enlightened day of the aforementioned ancillary surgical crutches. Weir's technique is rapid, simple, and practically bloodless. Staying under an hour of operating time, conserving blood, and respecting tissue made the operation safe in the old days. Good surgery did that.

I am in hearty agreement with the authors' thesis with the one exception which they probably can explain. I refer to panhysterectomy in ectopic pregnancy.

DR. A. W. DIDDLE, Knoxville, Tenn.—My comments regarding Dr. Johnson's informative study will be limited to the safety and the selection of patients for total hysterectomy, and carcinoma of the cervical stump.

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It is agreed that total hysterectomy can be made a relatively safe procedure. This impression is obtained from a study of two groups of women of nearly 700 each, recently treated by hysterectomy in two different hospitals in Knoxville. One group of women was cared for without an operative death as opposed to three deaths in the second group. It was apparent that the medical staff used more care in selection of patients for hysterectomy in the first than in the second instance. Surgeons doing the operations ranged from the comparatively inexperienced to the highly experienced in both series. All the hysterectomies done in the first hospital mentioned were either the total or the radical operation done for uterine cancer except for 23 of the subtotal variety. On the other hand, a third of the hysterectomies were subtotal and the remainder total in the second hospital.

The essayist's study shows that physicians of the Tulane staff were subjected to much experience in the use of hysterectomy. Several years were required to develop a consistent policy in its use. To the contrary, the process of education is still in its adolescence in some other communities. It is not my purpose to create controversy but to show that problems concerning simple hysterectomy do exist, why they exist, and to give two different ways they are being studied.

In the first instance medical standards were studied by the medical staff in each of seven different general, civilian hospitals located in either East Tennessee or Kentucky. It is estimated that the combined number of hysterectomies done in these hospitals in the last five years approximated the number done on the Tulane Service in the same length of time. A summary of the information from the various hospitals may be of interest to you.

In contrast to the indications reported by Dr. Johnson, indications for operation frequently were not precise. The process of selection of patients for hysterectomy was more of a problem than the operative technique or mortality and morbidity rates. Subtotal hysterectomy was commonly done and vaginal removal seldom in some institutions. Errors in the use of hysterectomy usually came from failure to consider the patient as a whole and its use for other than gynecologic disorders.

Error became less, however, total hysterectomy was used more often, and the incidence of vaginal hysterectomy increased through consultative services, educational programs, résumé of professional work, or a combination of the three. Opinion as to the use of hysterectomy was affected in large measure by training, experience, and by the institution in which one had worked. Presumably there are hospitals accredited for training without either sufficient clinical material, adequate supervision of trainees, or an established policy as to total versus subtotal hysterectomy and the use of the vaginal technique. Development of gynecologic surgical judgment was apparently hampered under these circumstances.

Another approach to the use of hysterectomy for benign genital disease is the psysiopathologic one proposed by John Burch and Lavely. Dr. Burch has kindly permitted me to show the accompanying table. It summarizes their ideas. The respective weight of the patient's function, needs, and pathology are not given in relation to the result produced by operation. It is expected that these relationships will vary for different women. For instance, reproduction might be of little or no importance to a para iii, aged 28 years. To the contrary this capacity may be very important to a nulligravida aged 38.

Prophylactic hysterectomy for uterine cancer after childbearing is completed has been suggested by some physicians because of the low operative risk. Yet actuarial studies by Dr. Margaret Martin at Vanderbilt University show that total hysterectomy for all women in the age range 35 to 45 years would prolong their life less than five months. Norman Miller, Burch, and others intimate that at the present time the indication "cancer prophylaxis" alone is insufficient reason to remove the uterus. This indication must be incidental to other indications to satisfy the patient's needs.

On the other hand, if simple hysterectomy is to be done we agree that total rather than subtotal is the procedure of choice. For instance, 4 per cent of 885 consecutive

patients treated at the University of Iowa for cervical cancer during 1926 to 1942 previously had had a subtotal hysterectomy. The corresponding figure for all women (992) with this disease treated in Dallas, Texas, 1936 to 1946, was 10 per cent. Among nearly 300 treated in 1949 to Sept. 1, 1955, at the East Tennessee Tumor Clinic the figure was over 4 per cent. These statistics tell their own story.

TABLE I. PATIENT'S FUNCTION, NEEDS, AND PATHOLOGY AS RELATED TO HYSTERECTOMY

PATIENT'S FUNCTION	PATIENT'S NEEDS	PATHOLOGY	TOTAL HYSTERECTOMY
Live	Life	Not threatening	Kills 2-5 per 1,000 Saves 20-25 per 1,000 from cancer
Physical health	Good	Impairs	Improve
Mental health	Good	Impairs	Improve
Reproduction	No more	Impairs	Destroy
Sexual	Normal	Unaffected	Unaffected
Menstrual	None	Excessive	Remove
Ovarian	Adequate	Unaffected	Unaffected
Support	Normal	Unaffected	Unaffected

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DR. FRANK SMITH, New York, N. Y.—There is one thing that occurs to me when I hear statistics quoted on the incidence of cancer occurring in the cervical stump. I would like once to hear a series broken down as to how many of these cervical stumps presenting cancer were in nulliparous or in virginal women. I think some of the old operators, who did total hysterectomies many years ago, reserved the privilege of retaining the cervical stump in nulliparous women where the cervix was perfectly clean and not diseased.

I think it is confusing in the statistics as presented, not only this morning but everywhere in such instances, unless the type of cervix which is left is considered. I might say, however, that for many years my policy has been total hysterectomy in all cases.

DR. HERBERT E. SCHMITZ, Chicago, Ill.—Sufficient evidence has accumulated so that we can once and for all bury the supracervical or so-called incomplete hysterectomy. I believe the additional evidence presented this morning is extremely important. There are two points, however, that have been emphasized that I wish to re-emphasize. Although in our clinic the incidence of carcinoma of the cervical stump is 4.5 per cent, I believe the incidence of cancer occurring in stumps is less than 1 per cent. When we make a fast ruling such as Dr. Johnson described, we must realize that there is a possibility of increasing the risk to the patient over and above what the risk would be of carcinoma developing in that stump.

We recently had a visitor from a neighboring institution who told us he was chief resident at that institution, and that they were never permitted under any condition to do supracervical hysterectomies. If they found pelvic endometriosis or pelvic inflammatory disease which was so extensive that it was beyond their ability in their stage of development as gynecologic surgeons, they did not dare back out of the operation but they would consult a staff member in the house, to have him come in, and if he of the attending staff could not complete the operation, at least they were relieved of criticism.

I believe that when we are teaching fourth and fifth year residents pelvic surgery, we are perfectly correct when we say to them, "You should not do the supracervical operation," but, on the other hand, your surgical procedure should never have a higher mortality than if you were not to do the complete operation. In this way they develop surgical judgment which is as important as surgical skill. I believe this should always be remembered, and I would compliment and shake the hand of an individual who, on my service, came to me and said, "I could not do that without increasing the mortality." We

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my We have shown in the Cook County Hospital in Chicago, where we analyzed 3,000 to 3,200 hysterectomies, that the mortality at that time, before antibiotics were available, in cases complicated by pelvic inflammatory disease was 2.5 per cent. Since 1939 there have been 32 supracervical hysterectomies among 1,000 total operations on my service with a mortality of less than 0.33 per cent. In those 32 cases there were definite reasons for the performance of the supracervical procedure.

DR. EMIL NOVAK, Baltimore, Md.—I do not believe in surgery by edict. Dr. Johnson dismisses very lightly the cliché which would naturally occur to everyone in such a discussion, that there is no place for the word "never" and "always" in the surgical vocabulary.

On the contrary I believe very firmly that nowhere in gynecologic surgery is there a more proper indication for individualization of treatment than in the problem under discussion. Everyone, including myself, is agreed that total hysterectomy should be done whenever possible, or, to put it another way, unless the hazard of doing it is definitely greater than that of leaving the cervix. I submit that even the most expert surgeon may occasionally encounter such a case, in which he could probably, with great difficulty and some hazard, remove the cervix with the uterus, but in which he honestly feels that from the standpoint of the patient, which ought to be the determining factor, the subtotal operation is the one for this particular patient. It is the patient's welfare and not the fact that the surgeon would like to boast of a proportion of 100 per cent totals that ought to count. I certainly do not object to the general principle advocated in Dr. Johnson's excellent paper, but rather to the inflexibility with which it is urged.

One would get the impression that if a resident at Tulane comes up against a case of large multiple and perhaps intraligamentary fibroids complicated by bilateral endometrial masses with extensive endometrial infiltration of the rectum, he would be scared not to do a total hysterectomy for fear of being courtmartialed. This may be an overdrawn illustration, but if such a case were operated upon by a resident of mine. I would be likely to pat him on the back and compliment him on his surgical judgment if he did a subtotal rather than a total operation. Moreover, though I have been doing hysterectomies for more than half a century, and though my preference is always to do the total operation, I hope the time will never come when, because of the local pelvic or the general constitutional condition of the patient (I feel that panhysterectomy involves the unwarranted hazard to the patient), I will not have sense enough to put my tail between my legs and settle for a subtotal operation. If this be treason, then make the most of it. Finally, I'll be right mad if anybody ever misquotes these comments and says I prefer subtotal to total hysterectomy because I certainly do not.

DR. JOHNSON (Closing).—I would certainly not take issue with any statement made by Dr. Novak. However, I might say it is true that our residents are told dictatorially that they have to do the total operation. I would like to explain, however, that our first year residents do practically no gynecology. Our second year residents operate with either one of the senior residents or one of the visiting staff. Our third year residents are given operative privileges, but with any difficult case they are always assisted by one of our senior visiting staff. That is why we feel that we can be dictatorial to the extent of saying "always" and "never."

We are not advocating total hysterectomies by every gynecologist; we do feel, as I brought out, that in teaching institutions, such as Tulane, they can be done safely.

In answer to Dr. Wetherell's question regarding hysterectomy in ectopic pregnancy, most of our ectopic pregnancies occur in the Negro race, and most of them are ectopic because of pelvic inflammatory disease. Total hysterectomy is done when pelvic inflammatory disease is bilateral. May I also point out, however, that unless the patients are in excellent condition a total hysterectomy is not done. A salpingectomy alone would be done in order to control bleeding from the ruptured tube.

CESAREAN SECTION AS THE METHOD OF CHOICE IN MANAGEMENT OF BREECH DELIVERY*

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A NUMBER of papers have been published during the past fifteen years discussing fetal and neonatal deaths associated with breech delivery. Some authors have considered only pelvic deliveries while others have included cesarean sections. Some articles have emanated from large obstetrical services, others from private practice. Comparison of the incidence of section in the various reported series is at best only approximate, but an estimate places the highest figure at 18.8 per cent and the lowest at 6.8 per cent.

Some of the articles in which cesarean sections are reported tabulate the indications for abdominal delivery. Most frequently recorded by the various authors are:

- 1. Contracted pelvis, disproportion, etc.
- 2. Elderly primiparity, maternal age, etc.
- 3. Oversized fetus, large infant, etc.
- 4. Placenta previa.
- 5. Prolapse of the cord.
- 6. Prolonged labor, uterine inertia, cervical dystocia, etc.
- 7. Pre-eclampsia, severe pre-eclampsia, eclampsia, etc.

Indications less frequently or occasionally reported include:

- 1. Cardiac disease.
- 2. Fibroid blocking pelvis.
- 3. Poliomyelitis with patient in respirator.
- 4. Postmaturity, overdue labor, etc.
- 5. Previous stillbirths.
- 6. Repeat sections.
- 7. Sterility, long-standing sterility, etc.

The first cesarean section to be performed at the Boston Lying-in Hospital on a patient with breech presentation was done in 1899. From that date through 1952, 159 cesarean sections have been done for breech delivery on 154 patients, 5 of whom were subjected to 2 sections, each with breech presentation. No claim is made that these necessarily include all breech births managed by section. It is probable that in some instances, at least, repeat cesarean sections may have been associated with unrecorded breech presentations. It is also probable that in some cases, at least, when sections were performed for such emergency complications as antepartum hemorrhage or uncontrolled pre-eclampsia, unrecorded breech presentations were involved.

^{*}Presented at the Sixty-sixth Annual Meeting of the American Association of Obstetricians and Gynecologists, Hot Springs, Va., Sept. 8 to 10, 1955.

The cases reviewed, therefore, are those in which the recognized factor of breech presentation contributed, in major or minor degree, to selection of abdominal delivery in preference to pelvic.

Our experience shows that all the indications mentioned by the authors cited, with the exception of poliomyelitis, are represented in the Boston Lyingin series. When these indications are analyzed it is evident that in many the deciding factor favoring abdominal delivery was a condition which could well have been the deciding factor even if a breech presentation had not been involved. Thus, placenta previa, prolapse of the cord, prolonged labor, certain cardiac conditions, severe pre-eclampsia, previous stillbirths, previous cesarean sections, and elderly primiparity, especially following long-standing sterility, may be proper indications for section regardless of presentation. At the same time, when the breech presents as a coexisting factor the evidence favoring abdominal delivery may be enhanced thereby. The scope of the present paper precludes an extended discussion of the conditions mentioned.

More worthy of detailed consideration are the sections done for the mechanical factors consisting of contracted pelvis, disproportion, and tumors or cysts blocking the birth canal.

Since 1882, when Sanger described the "classical" cesarean section, certain indications for abdominal delivery have been generally accepted. Implicit in most of these indications is the impossibility of delivery through the pelvis or the probability that the fetus cannot survive pelvic delivery.

Aside from the presence of tumors or cysts blocking the birth canal, the commonest mechanical indication for performance of cesarean section occurs when disproportion exists between the size of the fetus in utero and the size of the maternal pelvis. The "absolute cesarean pelvis" is easily recognized by ordinary clinical measurements. More frequent is the "borderline pelvis" which may allow the birth of a small infant, but which may cause obstruction to the passage of a large fetus. Decision as to the type of delivery in such a case may be properly left to await the results of a trial labor in cases where the occiput presents, with pelvic delivery anticipated if the forecoming head can be shown to pass through the narrow diameters as labor progresses but with the corollary that abdominal delivery will be selected if disproportion is demonstrated at the critical level.

Where the breech presents, however, such a trial labor is not feasible, since the aftercoming head does not come into congruence with the questionable diameters of the pelvis until the terminal moments of actual delivery, at a time when, if disproportion exists, the result of the extraction will be a dead fetus or a severely traumatized infant.

The factor of fetopelvic disproportion in breech labor has long been recognized. Before the American Association of Obstetricians and Gynecologists Skeel¹² stated in 1912, "So far as regards cesarean section for contracted pelvis in breech delivery one must lose or save his baby according to his judgment at the beginning of labor. If section is to be done at all it must be done before any labor test or any accurate estimation of the head has been made."

Newell,¹³ in 1931, discussing the indications for cesarean section, stated that in the primigravida if the breech is not in the pelvis at the beginning of labor cesarean section may properly be considered if the fetus is unusually large or if the pelvis is contracted. He emphasized, however, that the indication is not so much the breech presentation as the other factors in the case, such as disproportion of the child and the pelvis, early rupture of the membranes, and unsatisfactory dilatation of the cervix. He also stated that in the multipara cesarean section is practically never indicated for breech presentation per se in the absence of other indications.

Neither Skeel nor Newell elaborated on their conceptions of either the contracted pelvis or disproportion between the child and the pelvis, their criteria being purely matters of clinical judgment applied to the individual case.

In a paper published in 1940 discussing the management of breech delivery and the fetal and neonatal death rate associated therewith, we¹⁴ stated that among 500 uncomplicated pelvic breech deliveries of single mature infants in primiparas there had been 5 stillbirths or neonatal deaths resulting from misjudgment of fetopelvic relationship. During the period surveyed there had been 32 cesarean sections employed for uncomplicated breech delivery of single mature infants in primiparas with no fetal or neonatal deaths. Both the pelvic and abdominal series excluded all factors involving prematurity of the infant, multiple pregnancy, and significant complications of pregnancy and labor other than possible fetopelvic disproportion. In other words, the two series were regarded as basically comparable.

From the figures given it was computed that the incidence of cesarean section in 532 breech deliveries in primiparas had been 6 per cent. If the fetopelvic relationship in the 5 fatal cases in the pelvic series had been correctly assessed in advance 37 cesareans would have been done, making the incidence of section 7 per cent.

During the last twenty years increasing attention has been paid to radiographic study of the pelvis. This has been both qualitative, dealing with the architecture of the pelvis as a whole, and quantitative as regards the dimensions of the inlet and midpelvic planes. Since 1940 we have used a modified Thoms technique of isometric x-ray study of the pelvis and believe it to be of considerable value in recording the dimensions of the planes in question, which are quite impossible to measure by ordinary clinical methods. We do not, however, omit clinical pelvimetry and believe it to be more accurate than radiographic measurement of the intertuberous and posterior sagittal diameters of the outlet.

Fetal cephalometry in utero by means of the x-ray has not proved reliable in our hands, when, as is the case when the breech presents, the head occupies the fundus. We concur with Mengert in the belief that a clinical estimate of the fetal head as small, medium, or large is useful for practical purposes and believe that such an estimate is more accurate when the head occupies the fundus than when it lies in the lower uterine segment. We believe, moreover,

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that a flat x-ray film should be made whenever possible before cesarean section is performed for breech delivery in order to avoid the embarrassment of delivering a living hydrocephalic or anencephalic infant.

Indications for Cesarean Section in the Boston Lying-in Series

Our series of 159 cesarean sections includes 96 primiparous and 63 multiparous women. Tables I and II show the paramount indication or indications for section in those cases which were associated with significant complications of pregnancy or labor. These cases will not be further discussed since it is apparent that the factor of breech presentation played a secondary or tertiary role in the choice of abdominal delivery.

TABLE I. CESAREAN SECTIONS IN PRIMIPARAS IN CASES WITH SIGNIFICANT COMPLICATIONS

COMPLICATION	NO. CASES	PARAMOUNT INDICATION(S) FOR CESAREAN
Diabetes	1	Severe diabetes, cervix unfavorable for induction of labor
Hydramnios	1	Fetopelvic disproportion, age 38 years
Placenta previa	2	Placenta previa (2)
Prolapse of cord	1	Prolapse of cord in first stage of labor
Rheumatic heart disease	1	Superimposed pre-eclampsia
Toxemia (pre-eclampsia)	15	Mild toxemia, cervical fibroids (1) Mild toxemia, fetopelvic disproportion (7) Mild toxemia, age 43 years (1) Mild toxemia, infertile 10 years, age 34 years (1) Mild toxemia, infertile 10 years, age 38 years (1) Severe toxemia (3)
Tuberculosis, active	1	Severe toxemia, fetopelvic disproportion (1) None ascertainable from record

TABLE II. CESAREAN SECTIONS IN MULTIPARAS IN CASES WITH SIGNIFICANT COMPLICATIONS

COMPLICATIONS	NO. CASES	PARAMOUNT INDICATION(S) FOR CESAREAN
Diabetes	2	Previous neonatal death, fetopelvic disproportion (1)
		Severe diabetes, previous section anti-Rh titer (1)
Hemorrhage, antepartum	1	Persistent bleeding in labor, age 44 years (1)
Placenta previa	4	Placenta previa (4)
Prolapse of cord	2	Prolapse of cord in first stage of labor (2)
Rheumatic heart disease	2	Previous neonatal death, fetopelvic disproportion (1)
		Previous stillbirth, age 35 years (1)
Stone in common bile duct	1	Two previous cesareans, age 41 years (1)
Toxemia (pre-eclampsia)	3	Previous cesarean section (3)

Table III lists the paramount indications for cesarean section in otherwise uncomplicated breech delivery, i.e., in cases unassociated with significant complications of pregnancy or labor for which section might have been considered the method of choice for delivery regardless of presentation. It will be noted that the sections done in primiparas prior to 1940 and those done since 1940 are separately itemized for the sake of convenient reference in comparing the incidence of cesarean section in the management of all breech deliveries before and after the use of radiographic pelvic measurement became more or less a routine procedure.

Table III shows that, from 1940 through 1952, 39 primigravid women were delivered of single infants presenting by the breech for indications which are comparable to those used in the 35 cesarean sections done in primiparous women prior to 1940. Among the 39 cases one each was performed for pro-

longed labor without progress, fetal distress occurring in the first stage of labor, obstruction of the pelvis by the nonpregnant horn of a bicornate uterus, and a fetus which was estimated to be above the average size. The remaining 35 were sectioned because of estimated fetopelvic disproportion. These 39 cases will be discussed more fully later in this article, but are enumerated at this point since they constitute the group from which the thirteen-year cesarean rate in breech delivery will be computed.

TABLE III. PARAMOUNT INDICATIONS FOR CESAREAN SECTION IN OTHERWISE UNCOMPLICATED BREECH DELIVERY

	PRIM	IPARAS		
INDICATIONS	BEFORE 1940	1940-1952	MULTIPARAS	TOTAL
1. Miscellaneous				
a. Previous myomectomy	2	0	0	2
b. Prolonged labor	4	1	0	5
c. Rupture of membranes	1	0	0	1
d. Fetal distress	0	1	0	1
e. Failed pelvic delivery	1	0	0	1
2. Significant past history				
a. Previous cesarean section(s)	0	0	34	34
b. Previous stillbirth(s), etc.	0	0	9	9
c. Previous ruptured uterus	0	0	. 1	1
3. Obstruction of birth canal				
a. Bicornate uterus	0	1	0	1
b. Leiomyoma of uterus	1	0	0	1
c. Dermoid cyst of ovary	0	0	1	1
4. Elderly primiparity only	5	0	0	5
5. Estimated oversized fetus	3	1	0	4
6. Estimated fetopelvic disproportion	18	35	3	56
Fotal	35	39	48	122

Among the 48 sections performed for breech delivery in multiparas, 34 were done as repeat sections. In 17, or exactly half of these, there was evidence of contracted pelvis. In the other 17, where there was no evidence of contracted pelvis, the prior section had been done for causes unknown in 7, and for such individual and nonpermanent indications as abruptio placentae, prolapse of the cord, etc., in 10. In this category as a whole repeat section was done since it has not been service policy to allow breech delivery through the pelvis to take place in a woman who has had a previous section for any cause.

The 9 multiparous patients who were sectioned because of previous still-births or neonatal deaths showed clinically normal pelves in 5 cases and some type of contracted pelvis in 4. The paramount indication for section in most instances was essentially compassionate, based upon one or more preceding obstetric catastrophes.

The case in which cesarean section was done because of rupture of the uterus in a previous labor occurred in 1899. The patient had had two still-births and one neonatal death associated with her first three labors and the uterus had ruptured in the fourth. Her conjugata vera was 8.5 cm. Cesarean section was done in 1899 and yielded a living infant that weighed 8 pounds, 9 ounces. It is doubtful if such a train of events could be demonstrated in any obstetrical service today.

The case in which section was done in a multipara because of pelvic obstruction by an ovarian dermoid requires no comment as to the indication for abdominal delivery.

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Section was performed in 3 cases in the series of multiparas for estimated fetopelvic disproportion pertaining to the current pregnancy only. All 3 patients had given birth to living infants through the pelvis in previous labors; each, however, was believed to have a borderline pelvis for the fetus involved in the current pregnancy. Section in each case yielded a living infant larger than any previously delivered. This category illustrates the problem of the "dangerous multipara" in that section was chosen because of apprehension that pelvic delivery this time might result in obstetrical catastrophe

The 74 sections for uncomplicated breech delivery in primiparas shown in Table III include the cases from which it is proposed to derive our present incidence of cesarean sections among all uncomplicated breech deliveries in primiparas. The paramount indications listed have been chosen from study of the individual records. In many cases there was some multiplicity of indications in that elderly primiparity, an estimated oversized fetus, or both coexisted with some degree of estimated disproportion. Nevertheless, the cases have been tabulated in the light of what study indicates to have been the principal factor in choice of section. Table IV lists the frequency of the paramount indications.

TABLE IV. PARAMOUNT INDICATIONS FOR CESAREAN SECTION IN OTHERWISE UNCOMPLICATED BREECH DELIVERY IN PRIMIPARAS

	NUMBER	PER CENT
1. Miscellaneous indications	10	13.5
2. Elderly primiparity	5	6.7
3. Obstruction of birth canal	2	2.7
4. Estimated oversized fetus	4	5.4
5. Estimated fetopelvic disproportion	53	71.7
Total	74	100.0

Analysis of the 10 sections for miscellaneous indications shows that estimated fetopelvic disproportion played a minor part in the decision for abdominal delivery. The two women in whom section was done for the indication, previous myomectomy, were in the pre-1940 group. One had a normal pelvis clinically, while the other showed evidence of a contracted inlet, the diagonal conjugate being recorded as 10.5 cm. Two of the 5 cases in which sections were done for prolonged labor showed evidence of mild inlet contraction clinically, but the fact that all were allowed to undergo labor lasting from 11 to 56 hours indicates that fetopelvic disproportion was a secondary consideration only. One primigravida was operated upon at 36 weeks of pregnancy because of spontaneous rupture of the membranes 90 hours before operation, labor not having supervened. A living child that weighed 4 pounds, 11 ounces, was obtained. The patient with fetal distress in the first stage of labor had an adequate pelvis by both clinical and x-ray standards. The primigravida in whom section was performed for failure of pelvic delivery in 1937 had a pelvis deemed adequate by the x-ray standards then in use despite a diagonal conjugate measured clinically as 11 cm. After full dilatation following longstanding spontaneous rupture of the membranes it was found impossible to bring down the foot of a frank breech because of a very tight lower uterine segment.

Cesarean section was performed in 5 primigravid patients, it is noted, because of elderly primiparity. In this series a woman aged 35 years or over is classed as elderly. In the entire series 14 primiparous patients were in the elderly age group. Four of the 14 showed no evidence of contracted pelvis, while one showed a very mild degree of outlet contraction; hence the age

factor was the determinant in choice of section. In the other 9 cases there was evidence of contracted pelvis and, although some of the records indicate that the age of the patient was uppermost in the mind of the operator at the time of delivery, this group as a whole is classed with the cases of estimated fetopelvic disproportion.

In one case in 1915 the birth canal was obstructed by a leiomyoma. In a second case, occurring in 1950, there was obstruction of the pelvis by the nonpregnant horn of a bicornate uterus. The pelvis in each case was of normal dimensions clinically and it was adequate by x-ray examination in the second.

Disproportion as an Indication

The last two categories in this series include those cases in which the fetus was estimated to be of larger than average size and those cases in which the estimate of the pelvis indicated the probability of mechanically difficult delivery as the result of fetopelvic disproportion if birth through the pelvis should be attempted.

Herein lies a crucial point of judgment in the management of labor with breech presentations in primiparas. On the one hand the maternal pelvis may be adequate by all known diagnostic methods to allow safe pelvic delivery of an average-sized infant presenting by the breech but may be dangerous to the safety of the fetus if the latter is above average size. On the other hand the fetus may be estimated to be of average size or less while the pelvis may show one or more of its important diameters contracted to a degree which places it in a borderline category.

TABLE V. ESTIMATE OF PELVIC CONTRACTION (MOSTLY CLINICAL) PRIOR TO 1940

			NO. OF CASES
-	Promontory reached by prenatal vaginal examination		8
	Conjugata vera, measured, 8.25 and 10.5 cm.	2	
	Diagonal conjugate, measured, 8.75 to 11.5 cm.	6	
	Conjugata vera 10 cm. by x-ray		2
	Flat pelvis on basis of short external conjugate only		2
	"Flat pelvis" unverified		1
	"Justo minor" or "markedly contracted pelvis"		2
	Outlet contraction, intertuberous diameter 6.5 to 7.5 cm.		3
	Total		18

As previously stated, the estimate of an oversized fetus is, so far as we are concerned, still a matter of clinical judgment. In the 4 cases in this series in which section was done for this reason alone, the resulting infants weighed from 8 pounds, 2 ounces, to 9 pounds, 8 ounces. This observation does not disregard either the fact that excessive size of the infants was diagnosed in certain of the 53 cases of section primarily because the pelvic measurements were deemed inadequate or the fact that in one of the sections performed for elderly primiparity the infant proved unexpectedly to weigh 10 pounds, 6 ounces!

Discussion is now brought to a focus on the 53 cesarean sections for breech presentation in primiparas classified under the primary indication of estimated fetopelvic disproportion. Of these, 18 were performed between 1911 and 1940, mostly on clinical impressions, albeit several were subjected to study of the anteroposterior diameter of the inlet by the stereoroentgenometric method described by Johnson. Of the remaining 35, performed from 1940 through 1952, one only was not studied by the modified Thoms technique which the Hospital adopted in the former year. Thirty-four cesarean sections for breech presentation in primiparas who were evaluated

by x-ray prior to operation are therefore available to compare with a contemporaneous series of pelvic breech deliveries occurring during the same span of years.

Table V lists the factors, mostly clinical, on which the concept of contracted or borderline pelvis was based in the 18 cesarean sections prior to 1940.

Analysis of the cases listed in Table VI indicates that section was done electively in 11, or 62 per cent, before the onset of labor, while 7 patients, or 38 per cent, were in labor before section, the longest 20 hours prior to operation.

TABLE VI. SECTIONS BEFORE AND DURING LABOR

NO. OF CASES	TYPE OF CONTRACTION	BEFORE LABOR	DURING LABOR	DURATION OF LABOR
2	Conjugata vera (manual)	2*	0	None
6	Diagonal conjugate	3	3	3-20 hours
2	Conjugata vera (x-ray)	2	0	None
2	Short external conjugate	1	1	8 hours
1	Flat pelvis (unverified)	0	1	19 hours
2	"Justo minor," etc.	. 1	1	191 hours
3	Cutlet contraction	2	1	51 hours

*One patient sectioned two hours after rupture of membranes.

In the cases of elective cesarean section it seems obvious that the operators concerned were satisfied beforehand that section was the method of choice for delivery because of fetopelvic disproportion. One patient with a measured true conjugate of 8.25 cm. and one with a measured diagonal conjugate of 8.75 cm. were in the class with absolute indications for cesarean section.

In the 7 sections performed after the onset of labor, individual circumstances varied considerably. Each case may be said to have been re-evaluated after labor began.

Case 1.—Diagonal conjugate of 10.5 cm. After three hours of labor a section was performed for "cephalopelvic disproportion." The infant weighed 7 pounds, 6 ounces.

Case 2.—Diagonal conjugate not measured before labor. After thirty hours of labor the patient was found to show a "frank breech with edema of buttocks." There was "marked contraction of the pelvis with cavity quite small, D.C. 11.5 to 12." The infant weighed 9 pounds, 11 ounces, at birth but had not been estimated as above usual size preoperatively.

Case 3.—Diagonal conjugate not measurable before labor. After thirteen hours of active labor the breech was high, the os 3 to 4 fingers dilated, the diagonal conjugate 10.25 cm. The infant weighed 6 pounds, 2 ounces.

Case 4.—The only measurements recorded were intercristal, 26; interspinous, 24.5; and external conjugate, 16 cm. If any attempt was made to determine the diagonal conjugate it was not recorded. After eight hours of labor section was performed. The birth weight of the infant was 7 pounds, 11 ounces.

Case 5.—In the patient with a "flat pelvis, unverified," the external measurements were intercristal, 28; interspinous, 22; external conjugate, 22 cm. Although there is no record of the diagonal conjugate, these measurements do not suggest a small inlet. Nevertheless, the operative notes indicated that after nineteen hours of labor the breech was "high, the os almost fully dilated, the symphysis very high and the pelvis flat." The infant weighed 7 pounds, 14½ ounces, at birth.

Case 6.—The external measurements in this case were ample, save that the external conjugate was 18 cm. The promontory, however, was not felt on vaginal examination. After nineteen and a half hours of labor the note was made "os 2 fingers dilated, inlet markedly contracted." No measurements were quoted. The baby weighed 7 pounds, 11 ounces, at birth.

Case 7.—The external measurements of the pelvis were above normal save for an intertuberous diameter of 8.5 cm. After five and a half hours of labor the os was 3 fingers dilated. There was "no progress." The birth weight of the infant was 7 pounds, 4½ ounces, and the pelvis was classified as "android-funnel."

The 7 cases just cited have been reported in some detail because of the varying factors enumerated. In Case 1 it seems that decision to operate might have been made earlier in view of the contracted inlet. Case 2 involved a fetus of considerably greater size than normal; had it been smaller, successful pelvic delivery would have been probable. In Case 3 it is reasonable to ask why a diagonal conjugate of 10.25 cm. could not have been determined prior to labor. In Case 4 the obvious flattening of the pelvis based on an external conjugate of 16 cm. leads to questioning the absence of internal pelvimetry before labor. The details of Cases 5, 6, and 7 indicate an element of rationalization in the choice of cesarean section for delivery.

From 1940 through 1952 there were 35 sections in primiparas for delivery of the uncomplicated breech on the basis of a prima facie estimate of fetopelvic disproportion even though further analysis of the records indicates that in a few cases the final decision for abdominal delivery resulted from consideration of factors other than pure disproportion. Thus the only patient who was not studied by x-ray before operation was a woman of 43 in whom elective section was done because of her age and the fact that she had a pelvis of the funnel type showing an intertuberous measurement of 7.75 cm.

Based upon the x-ray reports of our cases a classification of pelvic adequacy for breech delivery through the birth canal has been made. This classification is provisional only for the purposes of the present study. It does not pretend to be quantitative as are the estimates of inlet and midpelvic capacities suggested by Mengert, but, in the cesarean series, at least, it can be shown that a high proportion of the pelves assigned to Classes 3 and 4, when worked out in accordance with Mengert's standards, prove to be in the group which show 90 to 85 per cent or less of the average capacities of the inlet plane, midpelvic plane, or both, and which therefore are dangerous for pelvic breech delivery.

The four classes are as follows:

- Class 1. Estimated adequate for breech delivery.
- Class 2. Estimated probably adequate for breech delivery.
- Class 3. Estimated doubtful or borderline for breech delivery.
- Class 4. Estimated inadequate for breech delivery.

Table VII shows the types of pelvis identified (according to the *principal* characteristic of each) and the classes to which they are assigned.

TABLE VII. TYPES AND CLASSIFICATION OF PELVIS

CLASS	GYNECOID	ANDROID	ANTHROPOID	PLATYPELLOID	OBLIQUE	TOTAL
1	4	0	0	0	0	4
2	0	0	0	0	0	0
3	10	3	2	0	0	15
4	7	4	1	2	1	15
Total	21	7	3	2	1	34

Table VIII shows the pelvic planes at which fetopelvic disproportion was feared in the event of delivery through the birth canal.

Tables VII and VIII are of no conclusive value to support or dispute the choice of section for delivery in these 34 cases. Nineteen patients were sectioned electively either before labor or immediately after spontaneous rupture of the membranes. Fifteen were in labor when cesarean was performed.

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The radiographic findings were probably decisive in 14 of the 19 elective operations and in 7 of the 15 cases in which labor was already established at the time of section.

TABLE VIII. PLANE OF ANTICIPATED DISPROPORTION

PLANE	GYNECOID	ANDROID	ANTHROPOID	PLATYPELLOID	OBLIQUE	TOTAL
Inlet only Inlet and	13	4	2	2	0	21
midpelvis Midpelvis	2	2	1	0	1	6
only	2	1	0	0	0	3
Outlet only	4	0	0	0 .	0	4
Total	21	7	3	2	1	34

During the years 1940 to 1952, inclusive, there were 279 uncomplicated pelvic breech deliveries of single mature fetuses and infants all weighing over 5 pounds, 8 ounces, or 2,500 grams. One hundred and sixty-two, or 58 per cent, of the patients were adequately studied by x-ray prior to delivery and can be classified according to class and type. Seven were studied by lateral films only; all were arbitrarily considered to be "adequate" and hence have been assigned to Class 1, but cannot be definitely typed. Table IX shows the types and classifications.

TABLE IX. TYPE AND CLASSIFICATION OF PELVIS IN PELVIC DELIVERY, 1940-1952

CLASS	GYNECOID	ANDROID	ANTHROPOID	PLATYPELLOID	OBLIQUE	UNTYPED	TOTAL
1	98	5	14	1	0	7	125
2	8	3	1	0	0	0	12
. 3	19	3	3	0	1	0	26
4	1	2	1	2	0	0	6
otal	126	13	19	3	1	7	169
Vo x-ray							110
Grand total							279

Table X compares the pelvic classifications in the series of 39 cesarean sections and 279 pelvic deliveries from 1940 through 1952.

TABLE X. COMPARISON OF PELVIC CLASSIFICATIONS IN THE PELVIC DELIVERY AND CESAREAN SECTION SERIES

	GYNECOID	ANDROID	ANTHRO- POID	PLATY- PELLOID	OBLIQUE	UNTYPED	TOTAL
Class 1							
Pelvic	98	5	14	1	0	7	125
Cesarean section	7*	0	0	0	0	0	7*
Class 2							
Pelvic	8	3	1	0	0	0	12
Cesarean section	0	0	0	0	0	0	0
Class 3							
Pelvic	19	3	3	0	1	0	26
Cesarean section	10	3	2	0	0	0	15
Class 4							
Pelvic	1	2	1	2	0	0	6
Cesarean section	7	4	1	2	1	0	15
No x-ray							
Pelvic	0	0	0	0	0	110	110
Cesarean section	0	0	0	0	0	2†	2†
Total	150	20	22	5	2	119	318

*Includes 4 cases, indication fetopelvic disproportion; 1 case each, oversized fetus, fetal distress, obstruction of pelvis.

†Includes 1 case, elderly primiparity and outlet contraction; 1 case, prolonged labor.

Table XI shows a high degree of confidence in allowing delivery through the pelvis to proceed when the pelvis was considered adequate (Class 1) or probably adequate (Class 2). It also shows the increasing frequency with which abdominal delivery was resorted to when the pelvis was considered borderline or doubtful (Class 3) or inadequate (Class 4).

TABLE XI. INCIDENCE OF CESAREAN SECTION, 1940-1952

CLASS	TOTAL DELIVERIES	CESAREAN SECTIONS	PER CENT CESAREAN SECTIONS
1	132	7*	5.3
2	12	0	0
3	41	15	36.6
4	21	15	71.4
No x-ray	112	2†	1.8
Total	318	39	12.2

*†See footnotes to Table X.

In Class 1, section was done in 7 patients out of 132 despite radiographic evidence of pelvic adequacy. In 4 the decision was based upon estimated fetopelvic disproportion. One patient showed a clinical intertuberous measurement of 8.5 cm. and a corresponding posterior sagittal diameter of 6.25 cm. Another showed an intertuberous measurement of 7.5 cm.; section was performed while she was in desultory labor after eight hours with ruptured membranes. This case resulted in the only maternal death in the entire cesarean series; she died on the eighth postpartum day of pulmonary embolism which followed dehiscence of the abdominal wound. The third patient was also sectioned after eight hours of labor, two hours after the membranes had ruptured, since the operator decided that inadequate progress had been made. The fourth case was that of a patient 42 years old in whom section was done for an estimated large fetus (which weighed 8 pounds, 2 ounces, at birth) and an inlet considered borderline because of an obstetrical conjugate by x-ray of 10.6 cm.

The 3 other sections in Class 1 were done for reasons other than disproportion. One was because of an estimated oversized fetus, the birth weight of which was 8 pounds, 2 ounces. In the second case, fetal distress was shown in the first stage of labor. The third was done at 33 weeks of pregnancy because of spontaneous rupture of the membranes in the patient whose pelvis was blocked by the nonpregnant horn of a bicornate uterus.

Fetal and Neonatal Mortality

Since the primary objective of cesarean section in management of breech delivery is to assure the birth of a living infant where reasonable doubt exists that safe delivery through the pelvis may be expected, the gross fetal and neonatal losses in the two series are compared in Table XII.

The corrections shown in Table XIII are obtained by deducting from both series only the fetal and neonatal losses due to intrauterine death prior to labor (i.e., the macerated fetuses) and the infants showing gross malformations incompatible with extrauterine life. All other deaths are ascribed to mechanical factors connected with delivery, none of which, in the 279 pelvic deliveries, could be ascribed to fetopelvic disproportion. It is of some interest to note that the highest corrected percentage of loss occurred in cases showing borderline rather than unfavorable pelves, as well as to note that the prediction of a favorable pelvis did not assure against fatality from mechanical causes. Whether or not performed for completely justifiable indications, the

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39 cesarean sections showed no avoidable fetal or neonatal deaths, the one fatality resulting from multiple congenital anomalies that could not be diagnosed before delivery by x-ray or any other means.

TABLE XII. GROSS FETAL AND NEONATAL LOSS, 1940-1952

		FETAL A	ND NEONATAL	DEATHS		1
	DELIVERIES	MACERATED	MALFORMED	MECHANICAL	TOTAL	PER CENT
Pelvic Series.—						
Class 1	125	2	4	4	10	8.0
Class 2	12	0	0	0	0	0
Class 3	26	0	0	2	2	7.7
Class 4	6	0	0	0	0	0
No x-ray	110	0	5	1	6	5.5
Total	279	2	9	7	18	6.5
Cesarean Section Se	eries.—					
Class 1	7	0	0	0	0	0
Class 2	0	0	0	0	0	0
Class 3	15	0	0	0	0	0
Class 4	15	0	1	0	1	6.6
No x-ray	2	0	0	0	0	0
Total	39	0	ī	$\overline{0}$	1	$\overline{2.6}$
Grand total	318	2	10	7	19	6.0

None of the 279 patients delivered through the pelvis died, while one maternal death occurred in the 39 cesarean sections. One death in 39 seems a high cost to pay for the privilege of adding 38 safely delivered infants to a series of 268 infants safely delivered by means other than cesarean section. It should, however, be remembered that the single maternal death occurred in a total of 159 cesarean sections rather than in the 39 cesareans performed since 1940. Nevertheless, the fact that this death occurred should keep us aware of the fact that even under modern conditions the operation carries with it risks to the mother which are considerably greater than those imposed upon a patient delivered through the pelvis.

TABLE XIII. CORRECTED FETAL AND NEONATAL LOSS, 1940-1952

	DELIVERIES	FETAL AND NEONATAL DEATHS	PER CENT
Pelvic Series.—			
Class 1	119	4	3.4
Class 2	12	0	0
Class 3	26	2	7.7
Class 4	6	0	0
No x-ray	105	1	0.95
Total	$\overline{268}$	7	2.6
Cesarean Section Series.			
Class 1	7	0	0
Class 2	0	0	0
Class 3	15	0	0
Class 4	14	0	0
No x-ray	2	0	0
Total	38	$\overline{0}$	$\overline{0}$
Grand total	306	7	2.3

By eliminating 11 of the 279 pelvic deliveries and 5 of the sections, one arrives at the incidence of cesarean section as the method of choice for management of uncomplicated breech delivery in primiparas as reflected from

the records of the Boston Lying-in Hospital from 1940 through 1952. The 11 pelvic deliveries eliminated are those which produced macerated and malformed products of conception; the 5 cesarean sections eliminated include one case of fetal malformation and 4 living infants that did not qualify as mature by virtue of weighing 5 pounds, 8 ounces (2,500 grams), or less. Since, therefore, 34 sections were performed to deliver 302 infants, the incidence of cesarean section in uncomplicated, single, mature, breech delivery in primiparas at the Boston Lying-in Hospital from 1940 through 1952 has proved to be 11.2 per cent. In the category of 268 pelvic breech deliveries no infant was lost because of fetopelvic disproportion.

Summary

Cesarean section may be the method of choice in management of breech delivery, depending upon a wide range of indications, most of which are relative rather than absolute. Certain of these indications are predicated upon disproportion between the fetus and the birth canal while others are not.

In general it may be stated that any significant complication of pregnancy or labor which would constitute an indication for cesarean section in the interests of a fetus in the usual cephalic type of presentation is equally or more valid as an indication for section if the fetus presents as a breech.

In the multipara delivery of the breech by cesarean section becomes the method of choice if the patient has lost one or more previous infants by pelvic delivery, or if she has been subjected to one or more previous cesarean sections.

Regardless of parity cesarean section may be the only way to secure the birth of a living child for the patient whose pelvis is obstructed by cysts, tumors, or congenital anomalies of the pelvic organs. Under such circumstances the indication for operation is absolute unless the obstruction can be displaced or removed.

In the primigravida the age of the patient, if 35 years or over, particularly if associated with a long history of marital infertility, may be in itself an adequate indication for section.

An estimate that the fetus in utero is of an appreciably larger size than normal, especially if the patient is primigravid and the fetus postmature, may be a proper indication for abdominal delivery even though the pelvis is believed adequate in its diameters for passage of a normal-sized infant. In the occasional multipara with mild pelvic contraction who has been delivered successfully of one or more small infants through the pelvis the estimate of an oversized fetus in the present pregnancy may make section the method of choice.

Experience indicates that in over seven-tenths of our cesarean sections for delivery of the uncomplicated breech in primiparas anticipated fetopelvic disproportion was the crucial factor in causing selection of abdominal delivery. Our experience also indicates that x-ray pelvimetry and pelvic evaluation together with careful clinical measurement of the outlet diameters afford a better guide for prognosticating fetopelvic disproportion than clinical pelvimetry alone.

Conclusions

1. Use of the x-ray to study the maternal pelvis and to measure the diameters of the inlet and midpelvic planes is the most accurate method now available for anticipating fetopelvic disproportion in cases of breech presentation. Such study should always be complemented by careful clinical measurement of the intertuberous and posterior sagittal diameters of the pelvic outlet.

2. Estimates of pelvic contours and diameters should be considered in relation to the estimated size of the fetus in utero. While a satisfactorily accurate method for measurement of the important diameters of the fetal head remains to be devised, the evidence by palpation of the size of the fetus as small, average, or large is of clinical value.

3. Largely because of the increasing use of x-ray studies, the incidence of cesarean section for delivery of the uncomplicated, single, mature breech in primiparas at the Boston Lying-in Hospital has risen from 6 per cent prior to 1940 to 11.2 per cent since 1940. During the latter period no fetal or neonatal deaths have resulted from misjudgment of relative fetopelvic propor-

4. Further study of inlet and midplane capacities by the method advocated by Mengert¹⁶ should be of value in acquiring a more accurate conception of borderline and severely contracted pelves.

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Discussion

DR. H. HUDNALL WARE, JR., Richmond, Va.—Dr. Goethals investigated carefully the records of 159 patients with breech presentations in an attempt to classify the patients as to indications for delivery by cesarean section, and found in many patients a combination of several factors which influenced the operator to select a cesarean section as the

In Table XI he has shown the increasing incidence of cesarean section deliveries in patients in whom the pelvis was considered borderline, doubtful, or inadequate. In a group of 132 deliveries in patients classified as having normal or adequate pelves, 5.3 per cent were delivered by cesarean section. In another group of 21 patients with small or inadequate pelves, 71.4 per cent were delivered by cesarean section.

Dr. Goethals and his associates are to be congratulated upon the accuracy of their estimates as to the size of the maternal pelves and the size of the fetuses, as shown by his statement that since 1940 ". . . no fetal or neonatal deaths have resulted from misjudgment of relative fetopelvic proportions."

We agree with the essayist "that any significant complication of pregnancy or labor which would constitute an indication for cesarean section in the interests of a fetus in the usual cephalic type of presentation is equally or more valid as an indication for section if the fetus presents as a breech."

We particularly want to emphasize the importance of radiographic study of the pelvis. The type of pelvis and the actual measurements are both important. We think the fetus extended in utero is usually more difficult to deliver vaginally than one of equal size which is well flexed. Clinical evaluation of the size of the fetus is a valuable aid in determining the method of delivery.

The essayist's incidence of cesarean section in 11.2 per cent of breech presentations is not excessive when one considers the increased incidence of breech presentations in elderly primiparas and the tendency to large babies in these patients.

In 1953, I reported before this Society 473 consecutive breech deliveries with no maternal mortality, and a corrected fetal and infant mortality of 2.11 per cent for babies weighing 1,814 grams or more. In 88 breech presentations delivered by cesarean section, there was no maternal mortality, and only one infant failed to survive. Irregularity of the fetal heart early in labor was the indication for cesarean section in this case.

DR. J. BAY JACOBS, Washington, D. C.—Dr. Goethals has made a very careful study of the incidence of cesarean section in breech presentation and has found it to be between 18.8 and 6.8 per cent. He also mentioned the fact that usually cesarean section is done for some indication that would require cesarean section regardless of the breech presentation.

In the multipara, of course, one is not too concerned about breech or the type of breech, unless there is a history of previous cesarean section, dystocia, stillbirth, or neonatal death. On the other hand, in the primipara one is more concerned. We know also that a frank breech is more difficult to deliver than a full breech. We would worry less if we could be assured of the patient's cooperation toward the end of her labor, so that with a frank breech we can take hold of the fetal hips and proceed with the extraction. The risk to the fetus is much greater if one has to disengage a breech that has been in sight for some time, and proceed to an extraction with a uterus that is probably pretty irritable and does not have much retained amniotic fluid. In this respect we must consider the amount of analgesia and anesthesia used and the time of administration, so as not to interfere with any cooperation on the part of the patient. A simple flat plate roentgenogram will reveal the type of breech.

Dr. Goethals has stressed the fact that x-ray pelvimetry, at the present time, plays a very important part in the management of these cases. Unfortunately, I do not think that we have any reliable means of determining the size of the fetal skull in a breech presentation. The steroroentgenographic method of Johnson is probably one of the most reliable methods for mensuration of a head in the fundus, but even then, since the head is not a perfectly spherical object, I do not think that one could determine its size accurately. We can determine the size of a pelvis and its architecture, however, by x-ray pelvimetry, and can also evaluate the outlet to some extent; the posterior sagittal diameter can be measured pretty accurately on the lateral roentgenogram. In this respect, I do differ with the essayist since this measurement can be made and should be taken into consideration, as well as the clinical interpretation of the transverse of the outlet.

It will be noted that in the last study, extending from 1940 to 1952, the incidence of cesarean section was doubled. In other words it increased from about 6 per cent to 11.2 per cent, and justifiably so, because one has now a more accurate and reliable estimate of the size of the pelvis. The figures presented portray a conservative trend and at the same time a very judicious one.

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DR. WILLIAM J. DIECKMANN, Chicago, Ill.—We owe a debt of gratitude to Dr. Goethals for his original publication sixteen years ago in which he showed that breech delivery need not be accompanied by a mortality of 30, 50, or even 100 per cent, as I have learned some doctors have. Dr. Goethals has not been vociferous enough since his first publication, or else the mortality from the breech delivery would be still less.

I cannot agree with him that x-ray pelvimetry will lower breech mortality. It has its place but he apparently attaches more significance to x-ray pelvimetry than we do.

Many reports have been published about the stillbirth and neonatal mortality but no one has studied breech babies 1, 3, and 5 years after delivery. This problem would be an excellent one for this society and it could be carried out by the establishment of a registry using a simple form for each breech delivery. At 1, 3, and 5 years the doctor would be reminded to fill out a simple form. At the end of 18 months, valuable data, heretofore unknown, would be available. At the end of 3 and certainly by 6 years, definitive data would be available for all types of breech delivery and their effect on the baby.

DR. HAROLD HENDERSON, Detroit, Mich.—Exhaustive studies of results in breech delivery have shown a steady improvement until, now, reports like those of Goethals, Dieckmann, Morgan, and others, show that a corrected mortality of less than 1 per cent in infants over 2,500 grams is possible. That these results are not obtained over the country goes without saying, because they are achieved either by, or under the direction of, our best obstetrical minds. When we have supplied the country with trained men from our good maternity centers, and when all women are taught that complete obstetrical care is a necessity, then, and only then, will the deaths from breech delivery approach the irreducible minimum.

This poses a problem to a society like this because here are the educators. We teach the students the mechanics of obstetrics and are responsible for the instruction of the residents. It is true that the number of breech presentations in a service such as my own is only between 90 and 100 a year, but all these cases may be used for teaching purposes. It is not the number of breech deliveries that a resident handles, but how well he is imbued with the correct technique of handling them. How often does the head of the department stand by, or scrub in on the complicated cases and do an "on the job" bit of teaching? How often after such a case does the instructor dust off the manikin and review the technical phases of the delivery with his interns and residents?

Since Dieckmann has recently suggested it, I can now reveal what I have kept as a closely guarded secret—that I have many times done an elective version to demonstrate the maneuvers that safely lead a breech through the birth canal.

I am not surprised at Dr. Goethals' results nor those reported by Dieckmann, Morgan, and others. More than 10 years ago I reported to the Michigan Society of Obstetricians and Gynecologists a personal series of 288 consecutive breeches, from 1929 to 1942, with a gross fetal mortality of 14.8 per cent. There were no maternal deaths and no ruptured uteri. The mortality in the nonviable prematures (0-1,500 grams) was 89.1 per cent, in the immature group (1,500-2,500 grams) it was 21.2 per cent, and there were 9 deaths in babies that weighed over 2,500 grams. Of these 9, 3 were monstrosities, 2 were macerated, one died before the onset of labor, and one was lost with what we then called hemorrhagic disease of the newborn. Of the 2 remaining deaths, one was a result of intracranial hemorrhage after a difficult breech extraction. This patient has since been delivered normally, which at least partially salves our conscience for a death obviously due to delivery. The other infant that died was easily extracted, the second of breech twins, the first of whom was born alive. It died in four hours but an autopsy could not be obtained, so our corrected mortality was slightly under 0.7 per cent.

The greatest improvement in a series such as this will come from prevention of prematurity, the answer to which we do not as yet have, from improved pediatric care, and from a full realization of the effect of analgesia and anesthesia on both mother and infant.

In our series there were only 4 cesarean sections, an incidence of 1.4 per cent. Two were done as repeat sections, one for contracted pelvis and one for rheumatic heart disease, an indication which we might now question in the light of Ullery's experience in Philadelphia, reported at our last meeting.

Cesarean section is not the answer to the breech problem but the latter may be part of several indications for abdominal delivery. If we are going to solve all our problems of dystocia by section, let us train midwives and surgeons and relegate obstetrics to the limbo of lost arts.

DR. GOETHALS (Closing).—I want to compliment Dr. Henderson on the low fetal and neonatal mortality rates he has had in his series. They are quite as good as those shown by any figures I know about. He also has a low incidence of cesarean section. They certainly are not surgeons out there in Michigan, not midwives, but obstetricians.

With regard to Dr. Dieckmann's remarks, he paid me an undeserved and, I think, an inadvertent compliment in either the July or August issue of the American Journal of Obstetrics and Gynecology, because he seems to think that we have as low a fetal and neonatal mortality in breech delivery as he has. I wish we did. He also said something about his use of x-ray. I rather feel that x-ray evaluation of the pelvis in breech delivery is more or less suggested by that old cartoon of World War I by Bairnsfather with the caption "If yer knows a better 'ole yer can go to it." In other words we have no "better 'ole" than clinical judgment unless some method of x-ray pelvimetry and cephalometry is going to lead us into a better eventual appreciation of fetopelvic relationships.

With regard to what Dr. Jacobs said, I played around with the Johnson method of intrauterine cephalometry in breech presentation in the early thirties, and could get a measurable diameter, usually the occipitofrontal diameter of the head, which proved to be fairly accurate in only about 62 per cent of the trials. We gave it up more or less by common consent and went back to the ordinary methods of clinical evaluation.

EXPERIENCE WITH RADIOACTIVE COLLOIDAL GOLD IN THE TREATMENT OF OVARIAN CARCINOMA*

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Iowa Hospitals)

OVARIAN cancer is the third most common malignant disease of the female genital tract, being exceeded in frequency by endometrial and cervical carcinoma. Two recent studies of ovarian carcinoma by Kerr and Elkins¹ and Randall² from the University of Iowa Hospitals have reported 5 year survival rates of 31.5 and 27.8 per cent, respectively. While these rates compare favorably with those in the experience of others, there were two aspects of this disease that have been most disappointing. One was the large number of patients found on the first examination to have advanced carcinomatosis. The other was the poor survival rate of 50 per cent encountered even in the favorable cases where the carcinoma was confined to the ovaries. Although the 5 year salvage rate in the more advanced stages has been definitely improved by the addition of external irradiation therapy, the survival rates in Stages I and IIA were not influenced appreciably.

It occurred to us that a cytologic study of peritoneal washings in patients with ovarian malignancy might be of value in detecting early spread. A project was thus initiated to determine if abnormal cells could be detected in the fluid removed from the peritoneal cavity or the cul-de-sac. The first part of the paper is concerned with the results of the peritoneal cytology study. Because of the findings the treatment of early ovarian malignancy has been altered. The second part of the paper describes the present method of management of ovarian carcinoma and summarizes our experience to date with radioactive colloidal gold therapy.

Methods

From January, 1952, to March, 1955, all suitable patients over the age of 35 undergoing diagnostic dilatation and curettage had cytologic studies of fluid aspirated from the cul-de-sac. A 13 gauge needle was inserted into the cul-de-sac and 25 to 75 ml. of normal saline was injected. The fluid was then aspirated and sent at once without preservatives to the laboratory. There, the cytologist centrifuged the recovered fluid, spread the sediment on a glass slide, and stained the cells by the Papanicolaou technique.

Since January, 1952, all suitable patients undergoing gynecologic surgery were used for the study of peritoneal cytology. As soon as the peritoneal cavity was opened, any free fluid (even though small in amount) was aspirated and transferred to a sterile flask. If the patient had ascites, the fluid

^{*}Presented at the Sixty-sixth Annual Meeting of the American Association of Obstetricians and Gynecologists, Hot springs, Va., Sept. 8 to 10, 1955.

was collected and studied but these results are not included in this presentation. In most instances free fluid was not present so the viscera were displaced and 100 to 125 ml. of normal saline was injected in the pelvic cavity and thoroughly agitated. The fluid was aspirated directly from the cul-de-sac with an Asepto syringe. Occasionally in a deep pelvis it was necessary to aspirate the fluid through a gauze sponge because of interfering loops of bowel. The fluid was then transferred to a sterile flask and prepared by the cytologist. Because of the significant number of specimens that contained no cells, the aspirations are now being done through a sheet of Gelfoam which is prepared and stained as a biopsy specimen. It is hoped this will improve the recovery of cells.

The cytologic criteria of normal or abnormal cells in peritoneal washings are much the same as for material from other sources. One difference, however, is the presence of mesothelial cells which may appear quite active even though benign. Abnormal cells indicative of malignancy are distinguished by the pleomorphic and hyperchromatic character of their nuclei. These may occur in groups or may be scattered individual cells found throughout the centrifuged sediment.

Results of Cul-de-Sac Aspirations

There were no positive cytologic findings in this group, probably due to the fact that the patients were selected on the basis of the symptoms of postmenopausal or functional bleeding, and had negative pelvic findings. This afforded a group of clinically negative controls. Nevertheless, there were three patients found to have suspicious cytology. One patient had adenocarcinoma of the uterus and an associated small Brenner-cell tumor of the ovary. The other 2 patients had functional uterine bleeding with no evidence of malignancy and no further investigation was carried out. In this series there were 2 patients with ovarian carcinoma who had had incomplete surgery performed elsewhere and had been sent to the hospital for further therapy; in each instance the cul-de-sac aspirations were negative. Exploratory operations have subsequently been done on both patients and no residual malignancy was found.

TABLE I. CYTOLOGIC FINDINGS: CUL-DE-SAC ASPIRATIONS

Total			247	
	Autolysis	3		+
	Only red blood cells	64		
	No cells	• 50		
Insufficient			117	
	Other benign cells	16		
	Mesothelial cells	83		
	Squamous	28		
Negative			127	
Suspicious			3	
Positive			0	

The smears were negative in 127 cases. The squamous cells present were undoubtedly scraped from the vaginal wall by the colpotomy needle. In 117 instances the smear was inadequate for interpretation since no cells were present or there were only red blood cells reported. Autolysis before fixation made 3 smears inadequate.

Because of the difficulty of recovering adequate amounts of the injected saline and the improbability of ovarian malignancy occurring in this type of patient, this phase of the investigation was discontinued in March, 1955.

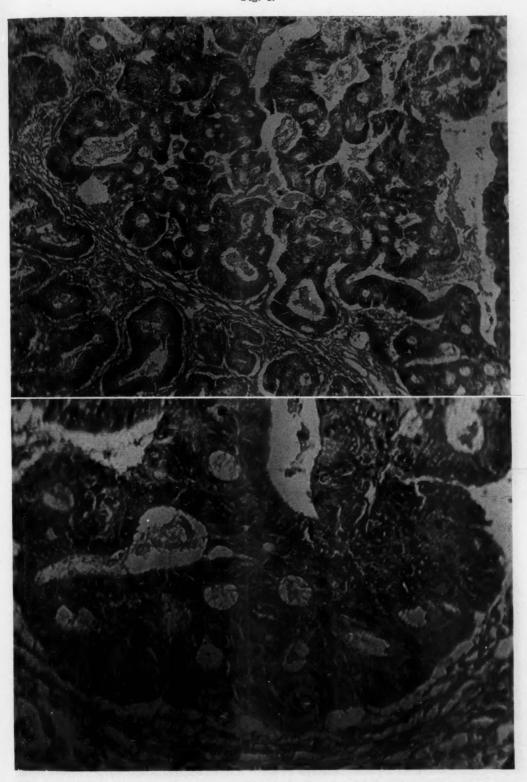


Fig. 2.

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Fig. 1.—Case 1. Low power; papillary serous cystadenocarcinoma with no clinical evidence of spread.

Fig. 2.—Case 1. High power; papillary serous cystadenocarcinoma with no clinical evidence of spread.

Results of Peritoneal Washings

There were 275 patients from whom peritoneal washings were available for study (Table II). Thirteen of the peritoneal washings were positive cytologically. Twelve of these patients had ovarian carcinoma and the thirteenth had a carcinosarcoma of the uterus. Of the 4 patients with suspicious cytology, 2 had ovarian malignancy, one had an endometrial cancer with peritoneal spread, and one had no demonstrable evidence of malignancy.

TABLE II. CYTOLOGIC FINDINGS: PERITONEAL WASHINGS

1	Positive	18		13
5	Suspicious			4
1	Negative			176
	0	Mesothelial cells	105	
		Macrophages	36	
		Other benign cells	36 35	
1	Insufficient			82
		Only red blood cells	78	
		Autolysis	4	
7	Total			275

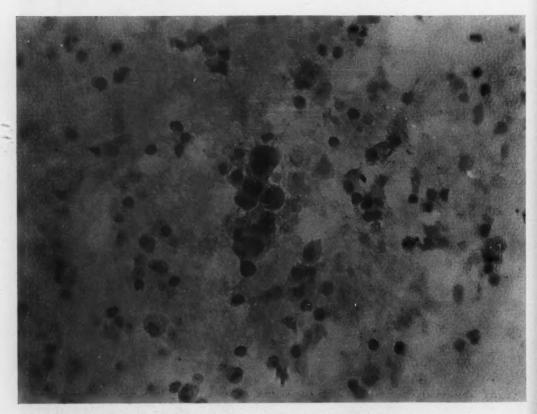


Fig. 3.—Case 1. A clump of malignant cells from peritoneal washings (oil immersion).

There were 176 patients with negative cytology, normal mesothelial cells, macrophages, and red blood cells being the only cells present in the smears. In 4 instances, ovarian carcinoma was present clinically. In 2 of the 4 patients, large amounts of ascitic fluid had been removed before the peritoneal

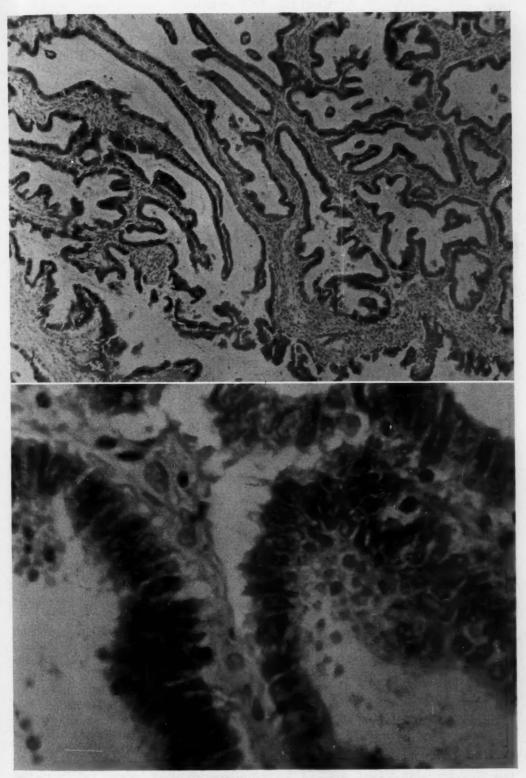


Fig. 5.

Fig. 4.—Case 2. Low power; intact tumor; papillary serous cystadenocarcinoma. Fig. 5.—Case 2. High power; intact tumor; papillary serous cystadenocarcinoma.

washings were obtained and this no doubt reduced the number of free cells that were present. In the other 2 patients abnormal cells should have been found.

Bleeding from the incision resulted in the presence of red blood cells exclusively in 78 smears and these were considered as inadequate for interpretation. Three of these patients had ovarian carcinoma. In 4 instances the cells had undergone autolysis and were inadequate for evaluation.

In Table III, of the 275 individuals whose peritoneal washings were studied, there were 35 benign ovarian tumors and in one instance abnormal cells were reported as being present. In 20 patients with histologically proved ovarian malignancy, 13 individuals had positive or suspicious cells present while in 4 cases no abnormal cells were seen.

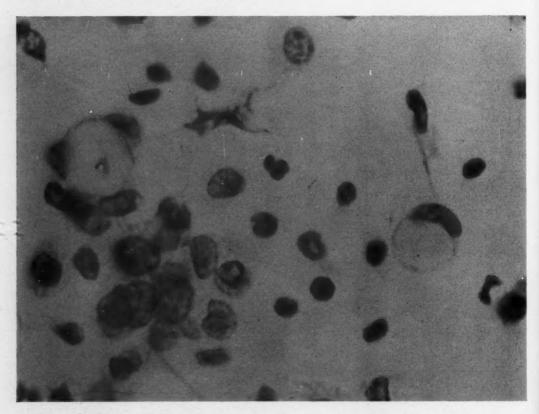


Fig. 6.—Case 2. Malignant cells found in peritoneal washings (oil immersion).

In the majority of the patients these cytologic findings were primarily of academic interest since the diagnosis was obvious from gross inspection. However, in 5 individuals with ovarian cancer there was no visible evidence of a break-through of the capsule, no free fluid, no omental or peritoneal implants, yet abnormal cells were present floating free in the peritoneal cavity. Three of these patients had a papillary serous cystadenocarcinoma and 2 a pseudomucinous cystadenocarcinoma. It was felt these abnormal cells might account for later recurrence encountered in certain patients with Stage I and IIA ovarian malignancy treated by adequate surgery. Figs. 1-6 show the histologic appearance of the tumor and the peritoneal cytology in 2 such patients.

TABLE III. CYTOLOGY: OVARIAN TUMORS (PERITONEAL WASHINGS)

Benign Cysts.—	
Positive	1
Suspicious	1
Negative	21
Insufficient	12
Total	35
Ovarian Carcinoma.—	
Positive	11
Suspicious	2
Negative	4
Insufficient	3
Total	20

Plan of Treatment

With the modified Heyman classification (Table IV) it is possible to stage cases of ovarian cancer accurately. Kerr and Elkins¹ showed the 5 year salvage with Stage I lesions to be 52.1 per cent, and 42.8 per cent in Stage II. Randall,² using a slightly different classification, recorded a 5 year survival rate of 63.3 per cent in Stage I and a 45.4 per cent survival in Stage II. Thus, in both series the 5 year survival, even in the most favorable patients who had an intact tumor with no clinical evidence of spread, was slightly over 50 per cent. The radiologists have shown that postoperative irradiation in these early cases apparently makes little difference in survival rates. They rightly ask what area of the abdomen should be treated since the tumor was completely removed and there was no clinical evidence of spread.

TABLE IV. MODIFICATION OF HEYMAN'S CLASSIFICATION OF OVARIAN CANCER

Stage	I:	Surgical removal of all the primary tumor and all visible metastases.
Stage	IIA:	Ascites with malignant cells or malignant cells spilled into the peritoneal cavity at operation.
Stage	IIB:	Partial or total removal of the primary lesion, but visible metastases remaining.
Stage	III:	Recurrence of malignant tumor following either operation or irradiation.
Stage	IV:	Inoperable tumor; exploratory or paracentesis only, distant metastases

The characteristics of Au¹⁹⁸ have been reviewed by Barnes,³ Sherman and associates,⁴ Andrews and co-workers,⁵ and Kniseley and Andrews.⁶ They have shown it to be a safe agent for the treatment of ovarian carcinomatosis with ascites. Fortunately, early in our cytologic investigation, abnormal cells were recovered in the peritoneal washings from a patient with a clinically intact ovarian carcinoma. It was postulated that these abnormal cells might give rise to the recurrences encountered in such favorable cases. It was felt that radioactive gold would be the ideal agent for the superficial irradiation of the peritoneal cavity and the destruction of any exfoliated cells. Thus the following treatment schedule for ovarian carcinoma was instituted and represents the first planned attempt to use Au¹⁹⁸ prophylactically in early cases.

Patients with Stage I and Stage IIA ovarian carcinoma were treated by abdominal total hysterectomy and bilateral salpingo-oophorectomy. Au¹⁹⁸ was given intraperitoneally on the fifth to the tenth day following operation (except for 4 patients treated at the time of operation). Each patient received from 150 to 200 mc. of radioactive colloidal gold. No additional external irradiation was employed. Patients with Stage IIB, III, and IV malignancies had as

much of the carcinoma removed as was deemed advisable. They received deep x-ray therapy to the pelvis and when possible were also given from 150 to 200 mc. of radioactive colloidal gold intraperitoneally. Recently the Stage IV patients have been divided into three categories on the basis of exploratory findings. The patient with relatively little upper abdominal spread receives external radiation and Au¹⁹⁸. The patient in good physical condition with extensive spread and marked ascites receives radioactive gold alone. The patients with extensive carcinomatosis and in very poor physical condition are not treated.

Material

Between February, 1951, and March, 1955, 66 patients with ovarian cancer have received radioactive colloidal gold. During this period 4 additional patients with ovarian malignancy and massive pleural effusion were given intrapleural Au¹⁹⁸. Eleven other patients with other types of genital malignancy have received gold therapy but are not included in this report. This is a report of our experience to date and sufficient time has not elapsed to determine 5 year survival rates.

There were 12 patients with an early ovarian cancer, Stages I and IIA; in contrast there were 41, or 62.1 per cent, with a hopeless metastatic spread to the omentum and peritoneal eavity (Table V). These findings parallel the experience of Munnell and Taylor⁷ and Randall and Hall.⁸

TABLE V. METHOD OF TREATMENT AFTER OPERATION

STAGE	1	AU198	AU198 AND X-RAY	TOTAL
I		4	0	4
IIA		5	3	8
IIB		1	8	9
III		1	3	4
IV		6	35	41
Total	-	17	49	66

Forty-nine of the patients were treated with a combination of surgery, external radiation, and colloidal gold. However, 17 patients received only colloidal gold therapy in addition to the surgical removal of all accessible malignancy. In the majority of cases, this was the planned method of treatment for the early cases. In certain patients with an extensive spread the radioactive gold was used alone to control formation of ascitic fluid.

The histologic findings are shown in Table VI. In this series there was a higher percentage of solid adenocarcinomas than cystadenocarcinomas which differs from the experience of Dockerty and Masson⁹ and others. This difference may be explained by the number of patients sent to the clinic with the expressed hope that radioactive gold might prove of value since the malignancy had not responded to surgery and external x-ray therapy. This series of cases was not weighted by a large number of the functional type of ovarian neoplasms; there was only one granulosa-cell carcinoma.

TABLE VI. PATHOLOGIC FINDINGS

Papillary serous cystadenocarcinoma	25
Pseudomucinous cystadenocarcinoma	7
Adenocarcinoma	27
Anaplastic carcinoma	6
Granulosa-cell carcinoma	, 1
Total	66

Method of Administration

Fig. 7 shows the apparatus used to protect the radiologist during the administration of radioactive colloidal gold. In most instances the radioactive gold was injected through a 13 gauge needle into the peritoneal cavity (Table VII). The material was administered usually 5 to 10 days following the operation except in patients receiving external irradiation when it was postponed until near the end of therapy. If ascitic fluid was not present, 1,000 ml. of normal saline was injected to be certain the needle was in the peritoneal cavity and to obtain distribution of gold throughout the abdominal cavity. In patients with ascites no saline was required and all avaliable fluid was drained prior to the injection of the gold. The patient remained in bed but was encouraged to change her position frequently to facilitate a wide dispersion. In a few instances a polyethylene tube was left in the peritoneal cavity at the time of operation for the purpose of injecting the gold at a later date. Our objection to this method of administration is that adhesions soon form that may prevent an adequate distribution and occasionally leakage occurs around the tubing. The initial dosage of Au¹⁹⁸ varied from 88 to 225 mc.; the majority of the patients received one injection. However, 8 patients received a second injection within 2 to 7 months.

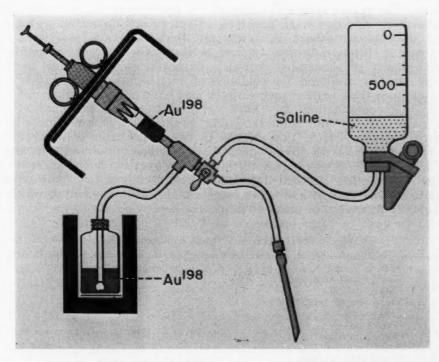


Fig. 7.—Schematic drawing of the apparatus used for colloidal gold administration.

TABLE VII. METHOD OF INJECTION OF RADIOACTIVE GOLD

Abdominal paracentesis	57
Polyethylene tubing	10
Injection into tumor	3
Injection at operation	4

Complications

The majority of the patients had no reaction from the Au¹⁹⁸. The individuals who were in excellent physical condition tolerated the procedure well but those with an extensive metastatic spread often tolerated the therapy poorly and on occasion the gold seemed to augment the patient's deterioration. Of the complications noted (Table VIII), the most frequent were mild nausea or vomiting, transient abdominal discomfort, and a mild temperature elevation. No serious infections were encountered. Leukopenia of a transitory type was observed in 4 cases. Bone marrow studies were done on 3 of the patients and the findings reported were normal. Four serious complications were encountered. In one patient, the gold was injected into the subcutaneous tissues of the abdominal wall and two months later a severe irradiation reaction of the skin occurred. The ulcerated skin did not heal and had to be excised surgically with subsequent healing of the area. Another individual, who was critically ill with marked ascites, ileus, and distention, developed a fecal fistula two days after therapy. No doubt the needle perforated a distended adherent loop of bowel. Rominger¹⁰ has reported a similar complication. Two patients treated by complete surgery, external irradiation, and colloidal gold therapy complained of mild nausea and vomiting, a dull aching sensation in the lower abdomen, and weakness one year after treatment. One of these patients developed an indefinite fullness in the lower abdomen. The pelvic findings confirmed the presence of an induration; x-ray and laboratory findings were negative. Exploratory operation was done on both of these patients because it was felt that they had recurrence. Each patient had a chronic adhesive type of peritonitis with thick edematous and adherent loops of distended bowel. Extensive biopsies and peritoneal cytologic studies disclosed no evidence of recurrence. Both patients have done well since their exploratory surgery and have had no further difficulties. Perhaps this complication may have resulted from the combination of external x-ray therapy and colloidal gold. Eight other patients have had exploratory operations from two months to two years after gold therapy and extensive adhesions with tissue edema have not been observed. In most patients, however, there was a gray metallic sheen over the bowel and peritoneal surfaces representing residual deposits of gold. Only a few filmy adhesions were noted. One patient had many large nodules in the omentum which were histologically proved to be areas of fat necrosis.

TABLE VIII. REACTION FROM RADIOACTIVE GOLD

None	45	
Nausea and vomiting	17	
Pain	14	
Elevation of temperature	11	
Leukopenia	4	
Weakness	3	
Chronic peritonitis	2	
Fecal fistula	1	
Severe skin reaction	1	

Results

When radioactive colloidal gold first became available, it was hoped that it would materially improve the 5 year survival rates with ovarian cancer. In the beginning, we were too enthusiastic concerning what colloidal gold would accomplish and every patient was treated; during the last several years a

more rational treatment policy has been established. It is too early to state whether these changes in therapy will improve our over-all 5 year survival. It is hoped that in the Stage I and IIA cases, surgery plus colloidal gold will materially improve our 5 year survival which in the past has been 50 per cent. To date only 12 patients with early ovarian cancer have been treated according to the method outlined (Table IX). All but two patients are living without evidence of recurrence two or more years after treatment. The two patients who died had been operated upon elsewhere and were sent to the clinic specifically for gold therapy. It is possible that the staging may have been incorrect.

Table IX. Survival of Patients Treated by Operation and Au¹⁹⁸ With or Without X-ray (November, 1950, to March, 1955)

	1 YEAR		1-2 YEARS		2 YEARS	
STAGE	LIVING	DEAD	LIVING	DEAD	LIVING	DEAL
I	_	_	3	-	1	-
IIA	1		1		4	2
IIB	1	2	3	1	1	1
III	_	2	1	1		-
IV	3	24	7	3	3	1

The majority of the patients with Stage IV lesions died soon after treatment. However, there are 3 patients who had an extensive spread who are living over two years after treatment without evidence of the disease. Seven patients are alive and comfortable one year after treatment. In this group of individuals it is difficult to determine whether Au¹⁹⁸ has been an important factor in their survival.

Seaman and associates,¹¹ Andrews and co-workers,¹² Müller,¹³ and Storaasli and others¹⁴ were quite hopeful that intraperitoneal gold therapy would prevent the formation of ascitic fluid and their reports were encouraging. In our experience, colloidal gold has diminished fluid formation in about half of the cases (Table X). In certain patients for a 2 to 4 month period the rate of fluid formation was diminished but then would gradually increase. In 12 cases it was felt the frequency of the paracentesis was decreased and in several patients the therapy was not required again. In 4 of the patients the therapy had no influence on ascitic fluid formation and 9 of the patients died within a month after treatment. It should be remembered that the presence of ascitic fluid is a rather late manifestation of ovarian malignancy, often occurring a few weeks prior to death. This makes the evaluation of the therapy most difficult.

TABLE X. EFFECT OF AU198 ON ACCUMULATION OF ASCITIC FLUID

Inhibitory	12
None	4
Unknown (death within 6 weeks)	9
Total	25

It is our feeling now that if the patient is in reasonably good physical condition and has marked ascites, gold should be used; however, if the patient's condition is deteriorating rapidly or she has marked ileus, gold therapy is contraindicated even for palliation.

Comment

The 5 year salvage in patients with ovarian cancer is lower than in cervical or endometrial malignancy. While there has been consistent improvement in the results of treatment during the last 20 years with uterine malignancies, this is not true with ovarian cancer. The principal reason for the poor treatment results encountered with this malignancy seems related to the inaccessibility of the ovary, preventing early detection by inspection or examination. The symptoms which bring the patient to the physician often develop only after extensive metastatic spread has occurred. In our material over 60 per cent of the cases had extensive metastatic spread when exploratory operation was performed.

It has been the hope of gynecologists that periodic pelvic examinations would prove of value in the earlier detection of ovarian cancer, yet there is no proof that this is true. It is of interest that 2 patients in this series had had regular semiannual checks by competent gynecologists, yet within a period of 4 to 5 months after the last pelvic examination were found to have a hopeless Stage IV spread.

It was hoped that, by cul-de-sac aspirations at the time of dilation and curettage, abnormal cells might be encountered and perhaps an early ovarian cancer would be detected. Our results in 247 cases were negative. The results with peritoneal cytology at the time of abdominal surgery have been encouraging since, in 5 patients with intact ovarian tumors, abnormal cells have been recovered from the peritoneal cavity. These dispersed cells may account for the relatively frequent recurrence reported for patients treated by total hysterectomy and ovariectomy. By the use of radioactive colloidal gold in such patients after their operation, it is hoped that a thorough irradiation of the entire peritoneal cavity will eliminate such abnormal cells, will not damage normal tissue, and will result in an improved 5 year salvage. The use of surgery, x-ray therapy, and colloidal gold may be of some value in the advanced cases especially as palliation.

Summary

- 1. In 247 patients, cul-de-sac aspirations at the time of dilation and curettage revealed no abnormal cells.
- 2. In 275 patients, peritoneal washings at laparotomy revealed abnormal cells in 17 instances. Fourteen had ovarian cancer, 2 extensive uterine malignancy, and one instance was a false positive.
- 3. Five patients with cystadenocarcinoma showed no clinical evidence of spread yet abnormal cells were found in the peritoneal washings.
- 4. Patients with Stage I and IIA ovarian carcinoma are now treated with abdominal total hysterectomy, bilateral salpingo-oophorectomy, and Au¹⁹⁸.
- 5. The remainder of the patients with ovarian carcinoma are treated with surgery, external irradiation, and radioactive gold when feasible.
 - 6. The majority of patients tolerate Au¹⁹⁸ with minimal complications.

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- 7. Colloidal gold is of value in controlling formation of ascitic fluid in certain patients.
- 8. Sufficient time has not elapsed to evaluate 5 year survival rates but results seem encouraging.

We wish to acknowledge the help and assistance of Miss Edna Pixley and Dr. James T. Bradbury in the preparation and interpretation of the peritoneal spreads.

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Discussion

DR. CLAYTON T. BEECHAM, Philadelphia, Pa.-In Table III the authors have listed one positive and one suspicious smear from the peritoneal washings in two cases of benign cysts. I should like to know if either of these patients have reported back with further disease? We have all had the experience of removing a unilateral cystadenoma, which the pathologist reports as benign but the patient soon after returns with malignancy in the remaining ovary.

What course would Dr. Keettel take in the following hypothetical case? In this patient a small amount of fluid in the pelvis at laparotomy contained malignant cells, but the unilateral cystadenoma in this young woman was diagnosed as benign after the study of multiple sections. I would like to have Dr. Keettel comment on whether he thinks the cytology of ascitic fluid is as reliable for demonstrating tumor cells as paraffin sections made from centrifuged fluid.

Dr. Keettel brought up the controversial point of postoperative x-ray in Stages I and IIA. As our radiologist puts it, "You have removed the target, where do you want me to aim?" For this reason the empiric use of radioactive colloidal gold in doses of 100 to 150 mc. has found favor in our clinic over the past four years. We are happy to find that Dr. Keettel's therapeutic plan at Iowa is essentially the same as the one used at Temple University Hospital.

DR. WILLARD ALLEN, St. Louis, Mo.-We began using radiogold for intraperitoneal metastases from ovarian malignancy several years ago and, as Dr. Keettel has said, we were quite optimistic originally. We were fortunate in having a few patients who had to be tapped every few weeks or so who, following injections of 100 to 150 mc. of radiogold, did not need to be tapped but very occasionally thereafter.

More experience, however, has shown us that such good results are not always obtained. The other disappointing aspect of the use of radiogold is that in the end, at least in all the patients we have treated, the disease progressed much as it does following x-ray irradiation. That is, small nodules begin to appear, then larger nodules, and finally, if the patient survives sufficiently long, the abdomen is filled with tumor.

We have come to the conclusion that intraperitoneal radiogold is a palliative procedure and not curative. I think, however, we should not condemn gold on the basis that it is only palliative. It seems to me to be far superior to x-ray therapy as palliation. With x-ray it often is necessary to irradiate the entire abdomen. When this is done serious trouble frequently arises because of diffuse irradiation of the intestines, and many patients, as we all know, are made quite sick. Radiogold provides diffuse irradiation and at the same time does not produce much sickness. After a few days the patient feels well and can usually go about her duties as usual.

The beneficial results obtained from radiogold raise a fundamental question. Does radiogold really destroy implants? I have had one opportunity of re-exploration in a patient who had previously received gold. This woman was operated upon on the Surgery Service with several liters of fluid in the peritoneal cavity due to implants from a malignant papillary serous cystadenocarcinoma of the right ovary. Implants were diffusely spread upon the surfaces of the peritoneum, according to the surgeons' statement. The large ovarian tumor was removed. A few days later gold was given intraperitoneally. The patient did not need to be tapped thereafter. About a year later a tumor appeared in the other ovary. At exploration, the right ovary was replaced by a malignant serous cystadenocarcinoma which unfortunately had invaded the posterior peritoneum. The peritoneal surfaces were very carefully inspected but no implants were seen anywhere except in the pelvic cavity where there were some small nodules. There was a multitude of gray spots on the surface of the intestines which would lead us to believe that the majority of the implants, all of which were small except in the cul-de-sac area at the time of the original operation, had been destroyed by the intraperitoneal gold. This points out, I think, that small implants may be eradicated by gold but larger ones, which I am sure were not more than 1 cm. in diameter, were not completely destroyed.

This leads us to the real problem, the one which has been brought out very specifically by Dr. Keettel. Should radiogold be used prophylactically in cases in which there are no obvious implants? I think we all agree that the patient who has implants should be irradiated, probably by gold. In the case without implants where the ovarian tumor is obviously malignant, radiogold should probably also be used prophylactically. Dr. Keettel's observation that tumor cells may be found in peritoneal washings, even though no visible implants are present, lends strong support to this idea. There might be some question, of course, in the occasional unilateral tumor, such as the granulosa-cell tumor or dysgerminoma in a young woman, where one would hesitate to give gold prophylactically because of the probable inevitable sterilization of the remaining ovary.

There are two questions which I would like to ask. Has Dr. Keettel had any experience in pseudomyxoma? Most of the time in this condition it would seem impractical because of the sort of collections here and there of the pseudomucinous material. Second, has he done any measurements on the disappearance of gold from the peritoneal cavity? We have the impression from a few observations of activity of ascitic fluid that the activity disappears very quickly after the injection. This, of course, makes us believe that the gold settles out on the peritoneal surfaces and exerts its influence there where we hope it may be effective in destroying the collections of tumor cells.

DR. HENRY L. DARNER, Washington, D. C.—I wish to ask the essayist a question and to speak about the relative merits of cell pack and cell washing. A patient was recently in one of our hospitals under the care of an internist for an active tuberculosis with a pleural effusion. The tentative diagnosis of the effusion was that it was tuberculous. Studies made on cell washings obtained by aspiration were negative. Cultures also were negative. Finally, a cell pack revealed malignant tissue which subsequently proved to be metastatic from an ovarian carcinoma.

A second patient in whom preliminary cell washings were not made proved to have a huge ovarian tumor. It was circumscribed with no evidence of metastases. We did a complete operation and obtained a diagnosis of cystadenoma—pseudomucinous in type, benign. Within a year an exploratory operation was performed on her in a military hos-

pital on Guam and the abdomen was found to be full of metastatic pseudomucinous cystadenocarcinoma. I wonder if cell washings at the time of the original operation might have put this case in the category of the malignant tumors.

DR. WARING G. COSBIE, Toronto, Ont.—There are two features of radioactive gold which should be kept in mind when we think of using it either with a hope of increasing the cure rate or as a palliative measure. The first is that gold is a relatively short-lived isotope and, therefore, does not present the serious problems of prolonged radioactivity either to the patient or to those who are in attendance on her. The second is that the depth penetration is slight as the activity depends on beta radiation rather than gamma radiation which is very slight indeed. As a result, effective irradiation is limited to about 6 mm.

It is an interesting speculation that the routine use of intra-abdominal gold might have a favorable effect in those cases where the tumor appears to be intact, but free cells are present in the abdominal or pelvic cavities. When, however, the implants are of appreciable size they will not be effected by this type of irradiation at all. Our experience in Toronto has been that this treatment is most beneficial in controlling the recurrence of ascites. Naturally, it is more effective still in controlling hydrothorax, as in the chest the serous surface is easier to reach. The multitudinous folds of the abdominal serosa present a factor much less favorable.

It is very doubtful if pseudomyxoma peritonaei would ever be effected by this form of irradiation because the mass of material would prevent effective irradiation of the secreting surface.

Therefore, in view of these considerations, it seems fairly obvious that, as with other methods of irradiation, in most cases the greatest usefulness of this agent will be to accomplish a degree of palliation, a possible prolongation of life, and a certain decrease in the suffering of the patient in the time of life that is thus given to her.

DR. LOCKE L. MACKENZIE, New York, N. Y.—At the University Hospital in New York City, whenever ascitic fluid has been taken, we have divided it into two parts, sending one to the cytology laboratory and the other to the pathology laboratory to be cut in cell blocks. I am sorry that I do not have the exact figures but my impression is quite definite that the diagnosis was made correctly more often by the cytological examination than by the examination of paraffin blocks.

In passing, the comment may be made that there is great difficulty in diagnosing malignant cells in ascitic fluid. There are so many macrophages, histiocytes, and other bizarre cells that it is very hard to determine which cells are malignant and which are not; this is particularly true in that the nonmalignant cells often appear in groups.

Papanicolaou's recent Atlas has done much to resolve these difficulties, but there is still room for much work in the morphology of malignant cells in body fluids.

I should like to ask Dr. Keettel one question. Does he have any idea of the mechanism by which malignant cells reach the ascitic fluid in so-called Stage I cases of carcinoma of the ovary when there is no evidence of metastasis?

DR. KEETTEL (Closing).—Dr. Beecham asked what has happened to the two patients with benign tumors who had a suspicious or positive cytology. Both have been followed and have shown no evidence of malignant recurrence. He also asked how much reliance can be placed on the peritoneal cytology. At the present time it is still considered an experimental tool; we have not had enough experience to date to state definitely its ultimate place in the management of ovarian malignancy. Dr. Elkins hopes that eventually we will be able to pick the cases suitable for colloidal gold therapy on the basis of the cytologic findings.

Dr. Beecham asked if making a paraffin block of the centrifuged sediment and sectioning this would improve our salvage of cells. We were concerned with the number of cases where only red blood cells were found. In obtaining the fluid from the peritoneal cavity, often the bowel and omentum interfered with the aspiration of fluid. When this

occurred the aspiration was done through a gauze sponge; we have wondered if this did not act as a filter reducing the number of cells recovered. Now we are aspirating the material through a Gelfoam sheet, and this sheet will be separately prepared and sectioned. We are hoping this will improve our recovery of exfoliated cells.

Dr. Allen asked about our experience with gold in patients with pseudomyxoma peritonei. We have treated two such patients without any benefit. With the extensive pockets of mucinous material that are present in such cases, an adequate distribution of gold is impossible. Dr. Allen asked about the rate of disappearance of gold from the peritoneal cavity. This has been checked on two patients and the majority of the gold disappeared from the peritoneal cavity in 24 hours.

Dr. Darner asked what types of malignant ovarian tumors are likely to shed the abnormal cells where the capsule was intact. All of our cases were either papillary serous or pseudomucinous cystadenocarcinoma.

Dr. Mackenzie asked where these cells come from if there is no break in the capsule. We do not know but it is postulated that it may be through lymphatic channels.

OBSERVATIONS ON THE MASSIVE STILBESTROL THERAPY OF ENDOMETRIOSIS*

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THE history of the treatment of endometriosis constitutes an excellent example of clinical research, i.e., the progressive application of therapeutic knowledge as the items of this knowledge were acquired through clinical observation.

Historical Review of Therapy of Endometriosis

In the beginning, endometriosis was considered a neoplastic process, possibly in some degree malignant, in very much the same way that we now think of pseudomyxoma peritonei. The concept of malignancy was heightened by the observation of the frequently invasive character of the lesion as seen especially in the "adenomyoma of the rectovaginal septum." On the basis of this concept the early treatment consisted of radical excision only, including the affected areas in hollow viscera. Unfortunately, this obsolete concept prevails to a considerable extent today, especially among non-gynecologists, so that it is by no means unusual to encounter cases in which resections of the ileum (frequently multiple), rectosigmoid, and bladder have been performed as elective procedures.

With the recognition that the tissue composing these lesions was in fact endometrium, and that the symptomatology and extension of the process were due to the cyclic endometriotropic and trophic factors of the ovarian secretion (at that time only vaguely identified), the concept of treatment by castration quite logically developed. It was promptly recognized that this, although effective, was far from an ideal treatment, since many of the patients were young and childless. By some strange distortion of logic, hysterectomy, leaving the ovaries and the endometriosis undisturbed, was practiced for a short time. Even within the last year I have seen two cases in which this procedure had been carried out, without relief of symptoms.

During the era of the castration concept, radiation naturally entered the field. Radiation, however, was not widely accepted because of two factors: first, that conscientious gynecologists were not willing to employ radiation without the definite diagnosis which could be made with certainty only by direct inspection and microscopic study; and, second, because the results obtained were in most cases far from ideal.

^{*}Presented at the Sixty-sixth Annual Meeting of the American Association of Obstetricians and Gynecologists, Hot Springs, Va., Sept. 8 to 10, 1955.

The next phase of treatment was based upon the recognition of several essential features of the situation:

- 1. That the process was not actually, and only very occasionally potentially, malignant, and hence in itself did not constitute a serious menace to the patient's life. The development of potentially lethal conditions such as intestinal or ureteral obstruction could in practice easily be recognized and appropriately treated.
- 2. That the prime therapeutic consideration in the uncomplicated case was in fact the relief of pain.
- 3. That the follow-up of untreated cases showed that in some instances at least the disease was of limited duration, even to the point of the subsequent restoration of fertility, with a probable activity of about nine years. We have observed seven untreated cases at irregular intervals for from 11 to 23 years. Two known pregnancies occurred, 10 and 13 years from the probable onset of the disease.
- 4. That most of the peritoneal areas affected by endometriosis lay within the sensory distribution of the presacral plexus, and that this plexus could be divided or partially excised without any demonstrable bad results, obstetric or otherwise.

From these considerations the use of presacral neurectomy was adopted as the best solution of the problem. Unfortunately, it rather promptly fell into disrepute because of certain misconceptions. The first of these errors was in regard to the sensory distribution of the plexus, which includes the uterus, the tubes, the cervix, to a variable extent the juxtacervical vagina, and most of the parietal and visceral peritoneum and extraperitoneal cellular tissue below the pelvic brim. It does not include the ovaries or the suprapelvic peritoneum. The second of these errors was in regard to the anatomy of the plexus itself. It is not a clearly defined structure, wholly visible. Since many of its component fibers are invisible, the only way to ensure an effective operation is to remove all of the tissue lying between the spinal structures (periosteum and lumbosacral ligaments) and the peritoneum (including the middle sacral vessels) and between the right and left common iliac vessels. The simplest way to accomplish this is to dissect bluntly and closely down the mesial side of the common iliac vessels until the spinal structures are reached; to extend this blunt dissection upward and downward along the common iliac veins for at least 3 cm. below the upper border of the lumbosacral joint; to join these two blunt dissections closely across the front of the spinal structures; and to clamp, sever, and ligate the upper and lower ends of the bridge of tissue so isolated. Incomplete removal of this mass of tissue leaves fibers of the plexus to continue to act as conductors of pain.

This technique was followed in our cases by complete relief of pain within the sensory distribution of the presacral plexus with one exception. The exceptional case was one with very atypical anatomy in the operative area, namely, a high bifurcation of the aorta and an inferior mesenteric vascular leash entering the pelvis along the right common iliac vessels and sweeping extraperitoneally across the entire field of the neurectomy. In this case the relief of pain was limited and "spotty."

The failure of presacral neurectomy to relieve pain in the ovary led to experimental ovarian neurotomy. This procedure was at first approached with some trepidation because it entails section and ligation of the ovarian artery and all of the veins of the ovarian leash. It was only through experience, long ago, with an identical procedure in the treatment of varicocele of the ovarian and pampiniform plexuses that we ventured to employ the operation. With the accumulation of cases it became evident that none of the hypothetical ill effects had occurred. Disturbances of menstruation were actually less frequent than in the cases of presacral neurectomy alone, and were always temporary. There was no increased incidence of retention cysts in the ovary. Five of our patients are known to have had successful pregnancies after bilateral ovarian neurotomy and presacral neurectomy. The follow-up of these cases showed no persistence of clinical evidence of endometriosis for longer than 3 years, most of the cell masses and adhesions having disappeared or been reduced to a minimum at the end of one year. In these cases actual endometrial cysts were removed at operation unless resection of hollow viscera would have been required.

The Results of Stilbestrol Therapy of Endometriosis

In 1948 Karl J. Karnaky informed me of the results obtained from massive stilbestrol dosage in cases of endometriosis. I first used this treatment on a patient who refused any form of operation. The results were so spectacular that I have been encouraged to continue to use it as the first line of attack in a series amounting to 33 cases to date. In all cases the cyclic pain was relieved. In all cases only actual cysts and some fixation of organs by adhesions could be palpated at the end of the three months' period of treatment. The definite cysts have persisted for a much longer time, but have eventually disappeared in most of the cases adequately followed. Eight of the 33 patients have since borne a child. Six of these had never before been pregnant. One case illustrates the paradoxical reactions of individuals which is so common in gynecic symptomatology and therapy:

This patient, at the age of 24, became pregnant two months after her marriage. Seven months after the termination of this pregnancy at term, she developed a typical massive peritoneal endometriosis with cysts of up to 2 cm. diameter in the cul-de-sac. She refused any form of operative treatment for twenty-six months, and was then placed on the Karnaky stilbestrol program. The relief of pain was complete. She menstruated twice after completion of this treatment and then became pregnant. Six months after this delivery the uterus was reposited from third-degree retroversion with no difficulty, and both ovaries were found to be free of adhesions. In spite of this, she gradually developed increasing pain in both ovaries which became so severe as to require bilateral ovarian neurotomy with presacral neurectomy twenty-three months after her second pregnancy. Both ovaries were the seat of active endometriosis, and there was a large unilateral hydrosalpinx from occlusion of the ostium abdominale by massive adhesions and old inactive endometriosis. All of her pain has been completely relieved and she is now, twelve months later, apparently pregnant again.

Diagnosis of Endometriosis

In making the diagnosis of endometriosis in the cases reported which were not operated on, the following syndrome was required in all of its details as a minimal standard:

1. The history of a "new kind" of dysmenorrhea, with a peritoneal or ovarian localization, usually in the cul-de-sac, referred to the rectum.

2. Persistence and progressive prolongation and spreading of this type of pain.

3. The touch-picture of progressive adnexoperitonitis: fixation of viscera by adhesions, obliteration of visceral outlines, etc., without fever or other systemic symptoms.

4. The finding of small, hard, globular nodules of various sizes among the dense adhesions. (Cysts of a diameter of 2 cm. or more cannot be accepted as a criterion.)

Technique of the Massive Stilbestrol Treatment

The technique which we have followed in these cases is based on the following schedule of dosage:

STILBESTROL 3 TIMES DAILY	
AFTER MEALS	NO. OF DAYS
1 mg.	5
2 mg.	5
3 mg.	5
5 mg.	5
10 mg.	5
15 mg.	5
25 mg.	- 5

The 25 mg. dosage is continued until the patient starts bleeding, when it is immediately raised to 50 mg. and then to 75 mg., 100 mg., and higher with each recurrence of bleeding. The total treatment period is 3 months.

We have found it better to discontinue the treatment abruptly without tapering off because the bleeding which ensues upon sudden total withdrawal is no worse than the recurrent bleeding which occurs in the stepdown withdrawal.

Conclusion

This is the original treatment as suggested by Karnaky, with some modification as to dosage. In view of the results obtained we have seen no reason to modify it, as for example, by the addition of other hormones. Without exception, in discussing unfavorable reports, dosages less than these had been employed. This report is submitted in the hope of inducing further study of the method.

Reference

Karnaky, K. J.: South M. J., Dec., 1948; Dec., 1952. J. A. M. A. April 9, 1949; Feb. 18, 1950 (Queries and Minor Notes). Texas J. Med. 44: 596, 1948. Am. J. Obst. & Gynec. 69: 573, 1955.

Discussion

DR. ROGER B. SCOTT, Cleveland, Ohio.—Any clinical use of hormones is for the most part empiric; the voids in our knowledge of hormone interrelationships are astounding. It is axiomatic that the administration of any hormone depresses the function of the parent organ. Therefore the administration of sufficient estrogen will depress ovarian function, be it a primary influence or be it secondary effect through suppression of the adenohypophysis. In any event, ovulation and cyclic menstruation no longer occur.

We are all familiar with the clinical improvement of external endometriosis which accompanies and follows a pregnancy. However, massive doses of estrogens do not exactly mimic the effects of a pregnancy. Progesterone, in many respects an antagonist of estrogen, and chorionic gonadotropins are not present for their unknown influence. The effects of massive doses of estrogens must differ in an exact sense from the full hormonal effects of a pregnancy.

Hormones are temporizing, not curative. Karnaky was impressed with the melting of adhesions; but neither does the fibrous cement disappear nor in the relatively few completely studied clinical experiments does the external endometriosis disappear. In a group of rhesus monkeys with experimentally produced endometriosis, reported last year at the Annual Meeting of the Association, the lesions did not disappear after large doses of estrogens; they remained and became hyperplastic after about two years. In addition the monkeys which had bleeding from the uterus also had evidence of simultaneous bleeding from the external endometriosis. Therefore we can postulate that ectopically located endometrium will bleed and disseminate whenever there is uterine bleeding, provided the ectopic endometrium is not too fibrotically encased.

An area of external endometriosis which is encased within an extensive fibrotic area does not receive and is not influenced by the full amount of circulating hormone. If it is deemed advisable (and in my experience this is rare) to administer estrogen for endometriosis it would be logical to administer it in such dosage that uterine bleeding will not occur. On the other hand, we have no assurance that large doses of estrogen, unopposed by other hormones, may not be harmful to the genital organs and the endocrine glands.

Despite our diagnostic acumen, let us be cautious in attributing the symptom of pelvic pain to endometriosis, even though it is clinically palpable. We are all familiar with the "doctor-shopper," the patient with the pelvic-pain syndrome. Just because we feel some endometriosis (or we think we do) this is no real reason to blame the pelvic discomfort entirely or even primarily upon endometriosis. As I have said before, if it were feasible to section serially the pelvic organs of all women 40 years of age with patent tubes, external endometriosis would be found in every instance. In a series of 516 patients at Johns Hopkins Hospital with histologically proved external endometriosis there was no pain, not even dysmenorrhea, in 139 instances, or 26.9 per cent. By and large ovarian endometriosis alone is painless; the uterus, with its periodic call for blood and its mechanical apposition to adjacent structures is generally a most important factor in producing the pain. Why preserve it when it has served its function? The discussant agrees with the tenet that a presacral neurectomy is indicated when dysmenorrhea is a symptom and when preservation of the uterus is clinically advisable. He does not agree with the principle that removal of the uterus and preservation of ovarian tissue is fuzzy thinking. It usually relieves the symptoms and averts premature castration.

A group of 98 patients were followed from nine months to fifteen years after surgical treatment of external endometriosis in which some ovarian tissue was preserved but reproductive function was not. Only four of these developed sufficient symptoms to warrant further treatment and in each instance castration by x-irradiation was administered.

Therefore (and I am the first to fall in line)—Vive la estrogen! Contrary to the French philosophy, a sensible approach to the use of hormones would be as follows (an approach which differs very little from the proper approach to our so-called vices): (1) maintain a critical attitude; (2) remain flexible in our treatment opinions, for something better may be now or potentially available; (3) avoid excesses. Practice moderation in all things; (4) realize that hormones are not the end.

DR. LOCKE L. MACKENZIE, New York, N. Y.—Dr. Cooke has given us some of the criteria for the clinical diagnosis of endometriosis. Brewer and Maher, however, have pointed out how difficult a diagnosis this is to make clinically. Sinclair diagnosed 103 cases, but less than three-fourths were confirmed by the microscope. Indeed, even when he diagnosed the lesion at the operating table, he was wrong in about a third of the instances.

Aside from the work of Karnaky, Hurxthal, and a few others, there are not many reported cases illustrative of the treatment of endometriosis with large doses of stilbestrol. I found a total of 128, to which must now be added Dr. Cooke's 33. About one-fourth were diagnosed histologically, the rest clinically. Over-all results were good in three-fourths, bad in one-fourth. However, some reports were 100 per cent good, others 100 per cent bad. It may be of interest that results were much better when endometriosis was proved by tissue sections. One is tempted to conclude that stilbestrol does not work in instances in which the lesion resembles, but is not actually, endometriosis. The number of cases is too small, however, and the results too varied for any statistical significance to be derived.

Side effects of stilbestrol therapy, the most serious of which are psychoses and severe hemorrhage, may be extremely troublesome. In about 44 per cent, they were so severe that treatment could not be continued, although Karnaky writes that Nembutal, given rectally, will control such effects within a week.

In 1925, Cotte described so-called "ovarian dysmenorrhea." Seven years later O'Donel Browne published his diagnostic sign, consisting of the reproduction of the typical menstrual pain by bimanual palpation of an ovary. It seems to me that this sign would be most difficult to evaluate, as I have yet to feel the ovary which could be thoroughly palpated without considerable discomfort and pain to the patient. In fact, whenever I have been successful in obtaining a good, solid grip on an ovary, the patient has invariably manifested a desire to be anywhere except on the examining table. In 1952, Wiseman and Thomas reported on 70 ovarian neurectomies; six months to a year later, 49 per cent were cured, 44.5 per cent improved, and 6.5 per cent unchanged. The small percentage of complete cures is due to the fact that some sympathetic nerve fibers reach the ovary with the ovarian branch of the uterine artery via the presacral plexus; thus, section of the infundibulopelvic ligament alone does not completely denervate the ovary. Therefore, if the operation is to be done at all, it is probably more logical to combine it with presacral neurectomy and the removal of whatever endometriosis is deemed advisable. There remains in my mind considerable doubt as to whether ovarian endometriosis per se is a usual cause of pelvic pain.

Finally, it may be said that animal experimentation fails to disclose any bad effects following ovarian denervation. Bernstorff and Bernstorff, working with rats, discovered no change in the ovary or uterus after the operation; estrus cycles continued as usual, and the ovary responded normally to gonadotrophins. However, they did notice an increase subsequently in the weight of the pituitary, and an augmentation in the potency of the gonadotrophins.

We need very much to know in exactly what type of endometriosis we should try surgery, estrogens, androgens, x-radiation, or nerve cutting. We may thus eventually hope to employ, in each case, the proper type of treatment.

DR. CHARLES P. MC CARTNEY, Chicago, Ill.—Although we have not utilized massive stilbestrol therapy in the management of endometriosis, we have had occasion to employ large doses of stilbestrol in a group of postmenopausal patients who have received complete irradiation therapy for squamous-cell carcinoma of the cervix. At the beginning of this study, we administered 750 mg. of stilbestrol daily. Currently these patients are receiving 1,250 to 1,500 mg. of stilbestrol daily with no demonstrable ill effect.

This therapy had to be discontinued in 25 per cent of the individuals in whom it was initiated because of nausea and vomiting. The critical daily dosage was 500 mg. It was found that if no difficulties were experienced by the time this level was reached, subsequent increases in dosage were well tolerated.

Seventy-five per cent of this group have taken from 1,000 to 1,500 mg. of stilbestrol daily without difficulty. One of this group who is taking 1,250 mg. daily has received stilbestrol for fourteen months and another individual who is taking 1,500 mg. daily has received this estrogen for eighteen months.

These individuals receiving stilbestrol experience an increased sense of well-being and have manifested a marked increase in appetite. Their breasts become moderately enlarged

and tender. One individual has experienced an enlargement of mammary tissue in one axilla which is a source of much annoyance to her. No significant increase in pigmentation has been noted.

These individuals evidence a weight gain which has varied from 8 to 14 per cent. This weight gain occurs during the first three months of therapy. After this period, the weight remains relatively stationary. No edema has occurred which could be attributed to the administration of stilbestrol although a salt-poor and low-potassium diet has resulted in an average 3 per cent weight loss in a two-week period. The serum electrolytes and the blood picture in these individuals have remained unaltered. Those individuals in this group who were subjected to diuretic studies displayed an inability to excrete water at a normal rate and evidenced an apparent increased sensitivity to intravenously administered Pitressin.

DR. ARTHUR HASKINS, Baltimore, Md.—Massive stilbestrol therapy is not a panacea for pelvic endometriosis. Dr. Karnaky has also expressed this opinion in his written publications concerning this relatively new method of endometriosis therapy. Those of us who have used this therapeutic regimen feel that it is merely an adjunct to the currently unsatisfactory treatment of this distressing disease.

If there be any unanimity of opinion as to the prophylaxis and treatment of pelvic endometriosis, it is in the phase of pregnancy. It has been the opinion expressed by many distinguished observers in gynecology that early childbearing may be useful in preventing endometriosis. It is also the considered opinion of many that, even after the disease is established, pregnancy, if it can be accomplished, is a useful medical treatment for pelvic endometriosis.

Since pregnancy is considered to be the best medical therapy for pelvic endometriosis, a pregnancy substitute or a pregnancy equivalent would be useful for those individuals in whom pregnancy cannot be accomplished or in whom pregnancy is not desirable. In my own experiences with massive stilbestrol therapy, it has been apparent that, under certain circumstances, this regimen is a pregnancy equivalent. There is uterine enlargement. There is increased mobility of the pelvic viscera. There are certain other changes occurring in the maternal organism that suggest a state of pregnancy in those individuals who have received large doses of stilbestrol.

Contrary to Dr. Cooke's practice, we have been giving this drug for a period of six months. As Dr. Karnaky has said, the treatment is not necessarily permanent, and many times recurrences, even in patients who are considered to be successfully treated, will occur in four to five years. However, a four- or five-year remission of the symptoms of endometriosis seems like a worth-while accomplishment to me. Repetition of the massive stilbestrol regimen in selected individuals, to my knowledge, does no harm.

DR. EMIL NOVAK, Baltimore, Md.—If my good friend, Willard Cooke, will not mind my saying so, I was sorry to hear him present this paper, because it does not seem to be in keeping with the critical scientific judgment he has always shown. Few will disagree that large doses of stilbestrol will often relieve the pain of endometriosis, but this is a very different question from that of the cure of this disease, and Dr. Cooke does not seem to have drawn the line very clearly. In his early work on this question, Dr. Karnaky was kind enough to send me some sections of the endometriosis from the small minority, as I recall it, of the cases in which such tissue was available for microscopic examination after treatment. I hope I am not misquoting him when I say that in most cases the diagnosis was on clinical rather than histologic grounds. In the few sections which I saw, there was still endometriosis present, and it would be difficult for me to believe that estrogen therapy of this sort would melt away, so to speak, an aberrant endometrium any more than it would the uterine mucosa proper.

Large doses of stilbestrol can, through the medium of the pituitary, practically abolish the function of the ovary. But the ovary soon bounces back if the estrogen is discontinued. As for its effect on the pain of endometriosis, this can probably be conceded with the added comment that pain is not nearly as frequent or troublesome a symptom as

many formerly believed, and numerous studies from various clinics have borne this out. There are few gynecologists who do not always have under their care certain patients in whom the palpatory evidence leaves no doubt of endometriosis, and yet who have little or no pain. If moderate pain is complained of, I would most often prefer simple analysis to hormones, though I have no quarrel with those who prefer the latter, whether in the form of estrogens or testosterone.

As to presacral neurectomy, there are few who do not consider this fully justified in properly selected cases. Without going into details, I wish only to register my comment that the operation has often been done on too slight provocation and therefore too frequently, that it is not quite all it has been cracked up to be, and that it is not altogether without hazard. The late Louis Phaneuf reported one death in his series, and I personally know of 2 instances of postoperative intestinal obstruction. No one that I know of would report the almost 100 per cent of successes reported by Cotle, the originator of the operation, with only 2 failures in 1,500 cases. This just doesn't sound right for such a subjective complaint as dysmenorrhea, and we cannot properly eliminate psychosomatic factors in the appraisal of results after presacral neurectomy any more than after the dilatation of the cervix which the surgeons of a preceding generation thought to be so effective in curing dysmenorrhea.

While there are all sorts of other angles, I shall comment on only one—that of the effort of some gynecologists, like the late O'Donel T. D. Browne, to differentiate an ovarian type of dysmenorrhea by simple pressure on the ovary. Most of you heard Dr. Browne's paper before this Association several years ago, and I got the impression that few of our Fellows were impressed by the views expressed. It seemed to be a flare-back to the old days of "ovarian neuralgia," and I question whether ovarian neurectomy has been or will be adopted by many of our colleagues.

DR. COOKE (Closing).—It seems that I had better restate my attitude. After all, this has been purely a report on a bit of clinical research which we have been encouraged to continue because of the rather surprising results obtained.

Of course there have been recurrences in these 32 cases, as has been mentioned. We have been obliged to operate in other cases, but not specifically for endometriosis. We have no explanation to offer for the rapid and usually permanent disappearance of the cell masses—it seems to be a process of atrophy and disintegration. Adhesions could not be expected to disappear, and they do not, except as a natural process over a long period of time. The cysts and the adhesions remain for a considerable period of time, and we have been obliged to operate once for a cyst which produced symptoms later.

One matter I omitted speaking of concerned the endometrial and ovarian biopsies in treated cases. There was evident a reversion to an infantile state in organs—a very remarkable thing to see.

I never think of endocrine dysfunctions or of the results of endocrine therapy without remembering a very remarkable statement which I heard made by a noted biochemist. He said, in discussion of the subject of the sex endocrines, "We should approach this subject in the proper frame of mind. That frame of mind is identical with the frame of mind of a puppy who was born on the back porch and had never been outdoors in his life. One very dark night the screen door was left unlatched and the puppy got out into the yard and ran into a tree. He investigated the tree to the best of his ability and he determined that it had a hard, rough surface which was nevertheless rather friable; that it was apparently cylindrical with a vertical axis; that irregular-shaped processes extended from its lower extremity and apparently entered the ground. There was distinct odor; and when a little breeze sprang up, there was a rustling noise which apparently emanated from the tree above his head. That is that puppy's total concept of a tree, and that, gentlemen, is our proper concept of the sex endocrines today."

COMPLICATIONS OF PREGNANCY AND NUTRITIONAL STATUS

I. Toxemias of Pregnancy*†

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ALTHOUGH experimental evidence derived from laboratory animals clearly demonstrates a relationship between maternal nutrition and reproductive performance, objective proof of a similar relationship during the gestation of human mothers is lacking. Indeed, reports attempting to relate maternal and fetal complications of human pregnancy to specific aspects of poor nutrition have been contradictory and largely inconclusive.

Within recent years several independently sponsored, intensive studies have been initiated in efforts to determine the role of nutrition in normal and complicated pregnancies through the application of more exact techniques. Our investigation, 13, 14 begun in 1947, yielded data based upon clinical observations, medical histories, food intakes, and seriatim microchemical determinations of hemoglobin, total serum protein, vitamin C, vitamin A, carotenoids, and alkaline phosphatase. This communication presents data concerning pregnancies complicated by pre-eclampsia and eclampsia in comparison with published data for subjects whose gestations were judged to have followed essentially normal courses. 14

The Study Group

The total of 1,064 subjects consisted of 378 white and 686 Negro women from three different socioeconomic groups: Group A—109 white and 544 Negro patients of an urban public clinic providing service to low-income and indigent segments of the population; Group B—33 white and 131 Negro patients of a private clinic serving families with moderate incomes; Group C—230 white private patients characterized as middle class with a few wealthy individuals.

In addition to the three groups, the total number of subjects included 6 white and 11 Negro women, of whom 5 were laboratory or clinic staff members and 12 were public clinic patients who, following uneventful pregnancies, participated in an investigation of blood components during five consecutive days in the puerperium.

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Of the 1,064 subjects, 160 white and 267 Negro women experienced apparently normal, essentially uncomplicated pregnancies and gave birth to living, evidently healthy, single infants weighing more than 2,500 grams at term. The other 218 white and 419 Negro women (approximately 60 per cent) experienced complications which, though often minor as far as life and health were concerned, nevertheless were considered to represent unusual or unfavorable experiences of gestation. Among the complications were 48 instances of pre-eclampsia and eclampsia, representing 4.5 per cent of the total group.

Since the subjects of this study were not chosen to represent a random sample of the Detroit population, or even of the clinical material of the hospitals participating in the investigation, the low incidence of toxemia may be a result of selective sampling. Similarly, the frequencies of normal and complicated pregnancies and toxemia portray the characteristics of one study group and do not present valid statistical evidence of the relationships of either race or living standards to the development of pre-eclampsia and eclampsia in a cosmopolitan community.

Pre-eclampsia and Eclampsia Group

To assess the significance of nutrition and its racial and socioeconomic implications in toxemia, clinical records, dietary ratings, and biochemical data of the 48 patients with pre-eclampsia and of 6 additional subjects from a previously reported study of plasma proteins in toxemia¹⁵ were chosen for comparison with those of healthy women who did not experience obstetric complications.

Race.—Of 49 patients with pre-eclampsia, 31 (63 per cent) were Negroes; 18 (37 per cent) were whites. Of 5 patients with eclampsia, 3 were white and 2 Negroes. Negroes composed 61 per cent of the patients who developed pre-eclampsia or eclampsia.

Socioeconomic Status.—Thirty-two of the instances of pre-eclampsia and the 5 cases of eclampsia occurred in subjects of the low economic group (68 per cent). Of these, 27 (73 per cent) were Negroes.

Parity, Age, and Multiple Pregnancies.—Fourteen white and 18 Negro women who developed toxemia (59 per cent) were primiparas 14 to 42 years old. Twin pregnancies occurred in 2 white and 2 Negro patients who developed toxemia.

Prenatal Care.—Prenatal care, judged by time of registration during pregnancy, regularity of appointments, and cooperation with obstetrical service was classified as "good" for 10 white and 12 Negro women who developed toxemia (42 per cent); "fair" for 3 white women and 14 Negroes (32 per cent); and "poor" for 7 white and 7 Negro women (26 per cent). The quality of prenatal care was not recorded for one white woman.

Nutritional Status

Although a considerable number of the subjects with toxemia represented underprivileged segments of the population, obvious clinical stigmas of malnutrition or frank deficiency disease were not recorded during physical examinations by the clinicians.

Pregravid Weight.—Among the 54 patients who developed toxemia, 2 white and 11 Negro women (25 per cent) were obese, i.e., their pregravid weight was 20 per cent or more above standard. The pregravid weight of 17 white and 21 Negro women conformed to normal standards. The pregravid height-weight measurements for 3 women were not known. None was known

to have been underweight before pregnancy. According to standard tables, 13 5.7 per cent of the white and 11.9 per cent of the Negro women studied who did not have complications of pregnancy were more than 20 per cent overweight; 1.0 and 2.3 per cent of the white and Negro women, respectively, were more than 20 per cent underweight.

Pregnancy Weight Gain.—Weight gains of 25 to 50 pounds during pregnancy were recorded for 11 white and 11 Negro women (43 per cent) who developed toxemia; 3 white and 7 Negro women gained less than 20 pounds.

Among women whose gestations were uncomplicated, gains were recorded of as much as 55 pounds for Negro and 43 pounds for white women; for 124 white and 162 Negro women whose pregravid weights were within ± 20 per cent of height-weight standards, the median weight changes were 23 and 24 pounds, respectively.

Food Intakes.—Dietary evaluations¹³ for 46 subjects who became toxemic during pregnancy indicated that 10 Negro and 4 white women had low or inadequate diets. Nine white and 20 Negro women were scored 60 per cent of adequacy or above, and one white woman had a dietary rating of 90 per cent. The median ratings for Negro and white women were 64 and 63 per cent, respectively. The median ratings for white and Negro women whose pregnancies were uncomplicated were 74 and 64 per cent, respectively.

Biochemical Assessments

Blood Sampling.—Peripheral blood samples were collected and analyzed by microchemical methods.16-21 Approximately 0.3 ml. of blood was drawn by finger puncture and hemoglobin and serum protein were determined immediately after collection and preparation of the samples. Samples and protein-free filtrates of serum were prepared and measured into microtubes which were stored at -30° F. for determinations of vitamin C, alkaline phosphatase, vitamin A, and carotenoids.

Results and Comment

The 49 cases of pre-eclampsia and 5 cases of eclampsia present typical examples of the true toxemias of late pregnancy with a preponderance of primiparity and high incidences of multiple pregnancies, pregravid obesity, and excessive gestational weight gains which are characteristic of this disease. Sociologic characteristics of the group support the generally accepted belief that although toxemia is no respecter of social class, low economic status and inferior prenatal care are somehow associated, to justify Whitacre's designation of the pre-eclampsia-eclampsia syndrome as "a disease of indigents."

The preponderance of Negro subjects in the toxemia group, though not a valid sample of the population, complements other reports^{22, 23} that racial factors, perhaps dietary, perhaps genetic, are also involved in the epidemiology. Nelson's²⁴ report on a survey of a presumably homogeneous population at Aberdeen denies a predisposition to pre-eclampsia for inferior socioeconomic status. Nevertheless, it seems abundantly clear from our own studies and the evidence of others that racial factors must be considered in comparisons of the incidence of toxemia in different geographical areas with differing ethnic compositions and widely disparate living habits. Biochemical and dietary data from our study of nutrition in uncomplicated pregnancies support the views of others regarding the distinctly inferior nutritional status of underprivileged subjects, particularly Negroes. Ross²³ presented evidence to support his opinion that socioeconomic, racial, and dietary factors contrive to make the "Late Toxemias of Pregnancy: Number One Obstetrical Problem of the South."

While most clinicians long have been convinced of these associations by prima facie evidence, objective proof, supported by data from suitably controlled investigation, is still scant. A basic handicap to our understanding is the lack of broad nutritional studies of healthy individuals before, throughout, and after uncomplicated pregnancies. Our data have shown that even in apparently normal pregnancies the blood levels of various nutrients fluctuate and wide variations occur among individuals, often approaching perilously near critical danger levels. These wide ranges under normal conditions emphasize the fallacy of pooling isolated, random chemical determinations from unselected subjects and establishing criteria for normalcy upon massed averages.

The study reported here involved intensive investigations of a small group of subjects from whom 3,766 maternal blood samples were obtained and subjected to a limited number of biochemical tests. It should be regarded as purely exploratory and the results demonstrate that nutritional assessment is as far from simple for the biochemist as it is for the clinician, each of whom possesses few adequate yardsticks of nutritional inadequacy except the presence of frank deficiency disease. Clinical criteria of deficiency, such as the gingival, lingual, ocular, and dermatologic stigmas emphasized by Tompkins^{25, 26} are generally unrecognized or are overlooked. Darby and associates⁴ showed that it is difficult for clinicians even to differentiate obesity resulting from nutritional inadequacy from that which might be conditioned primarily by endocrine aberrations in the presence of adequate food intake. The same quandary applies to judgment of nutritional status of the subject who is "underweight" by height-weight standards or by the subjective appraisal of the medical examiner. The importance of establishing objective criteria for assessing the nutritional significance of pregravid weight and weight gains during pregnancy and their relationships to the incidence of toxemia is obvious. Darby concluded:

There are no means of fixing real values for such attributes. The decision as to diagnosis is subjective and reflects the whole background of the individual physician-observer. The fact that different observers record varying incidences of diagnoses produces a large doubtful zone where evidence of manifest "deficiency disease" is not overwhelming.

In spite of many acknowledged weaknesses in our ability to assess nutrition, clinically or chemically, the microchemical blood determinations in preeclampsia and eclampsia showed trends which appear to be significant in comparison with the results of the same analyses of blood obtained from women whose pregnancies were uncomplicated.

Hemoglobin.—Levels of 10 to 12 Gm. of hemoglobin per 100 ml. of blood generally are regarded as the lower limits compatible with health during the reproductive cycle. Dieckmann and Wegner^{27, 28} and Sturgis²⁹ regarded hemoglobin levels below 10 Gm. as diagnostic of anemia. In obstetric practice levels of 10 Gm. or below are generally accepted as demanding active therapeutic measures to correct "anemia" but hemodilution from increased blood

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volume occurs progressively throughout pregnancy; hence declining hemoglobin concentration does not necessarily reflect iron or protein deficiency. True anemia, however, as a consequence of fetal demands, inadequate intake, or defective assimilation may occur and presents definite nutritional implica-The extensive literature relating hemoglobin levels in pregnancy to diet, race, sociaeconomic status, and other factors was reviewed in earlier publications.13, 14

Fig. 1 portrays the medians and ranges for hemoglobin during the courses of uncomplicated pregnancies among white and Negro women. The curves illustrate the usual physiologic trend of hemoglobin levels consequent to progressive hemodilution ante partum. In Negroes the median course downward parallels the curve for white women at a lower level (approximately 1 Gm. per 100 ml.) and the range is wider and below that for white women.

Table I gives the median concentrations of hemoglobin in white and Negro women with pre-eclampsia and eclampsia during the last trimester of pregnancy and post partum in comparison with concentrations at the same intervals in women whose pregnancies were uncomplicated. The table itemizes the percentages of hemoglobin determinations below 10 and 12 Gm. per 100 ml. for both groups.

TABLE I. HEMOGLOBIN LEVELS DURING UNCOMPLICATED PREGNANCIES AND PREGNANCIES COMPLICATED BY PRE-ECLAMPSIA AND ECLAMPSIA (GM. PER 100 ML. SERUM)

	WHITE	WOMEN	NEGRO	WOMEN
	NORMAL	TOXEMIA	NORMAL	TOXEMIA
Seventh Month.—				
Samples	83	6	90	16
Median	12.1	12.0	11.1	11.0
Per cent below				
10 Gm.	1	0	10	25
12 Gm.	43	50	77	69
Eighth Month.—				
Samples	132	11	145	27
Median	11.8	12.8	11.1	11.8
Per cent below				
10 Gm.	4	9	14	7
12 Gm.	58	36	78	59
Ninth Month.—				
Samples	205	22	176	33
Median	12.2	11.9	11.4	12.0
Per cent below				
10 Gm.	1	4	12	15
12 Gm.	41	54	67	48
Post Partum.—				
Samples	140	19	190	27
Median	12.3	10.8	12.2	11.5
Per cent below				
10 Gm.	7	21	7	22
12 Gm.	41	79	45	63

A downward trend in median hemoglobin concentration from the eighth month through the postpartum period is evident for white but not for Negro women with toxemias. The Negro women who had toxemia, as did those who had normal pregnancies, showed lower median concentrations and generally lower ranges of concentration than the levels in white women. Toxemia in both white and Negro women was associated with larger percentages of hemoglobin determinations below 12 Gm. and below the critical level of 10 Gm. per 100 ml.

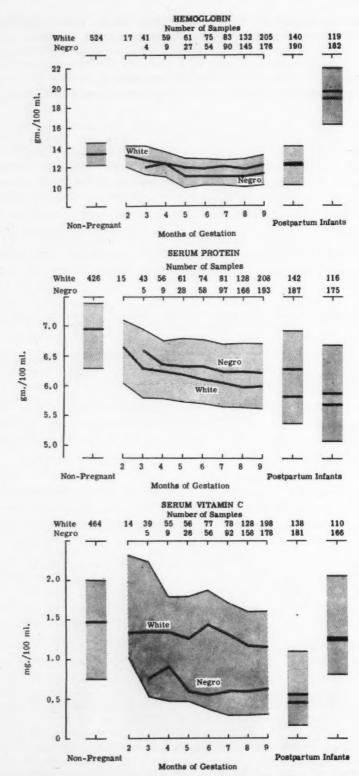


Fig. 1.—Median levels of hemoglobin, serum protein, and serum vitamin C of white non-pregnant women and of white and Negro women during normal gestations, after delivery, and of their newborn term infants. The tenth to ninetieth percentile range for the combined racial groups serves as a standard for normality.

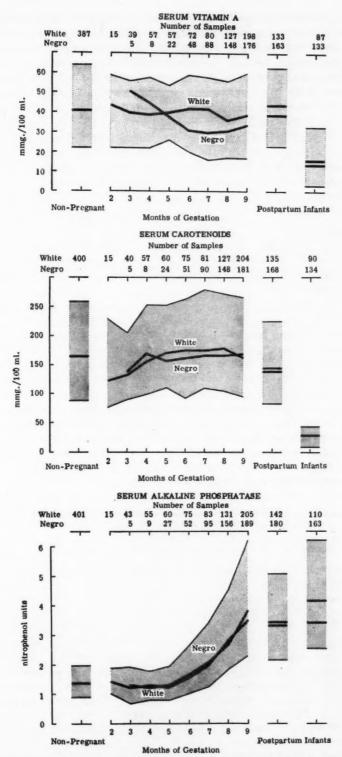


Fig. 2.—Median levels for serum vitamin A, serum carotenoids, and serum alkaline phosphatase of white nonpregnant women and of white and Negro women during normal gestations, after delivery, and of their newborn terms infants. The tenth to ninetieth percentile range for the combined racial groups serves as a standard for normality.

The lower concentrations of hemoglobin in Negroes, also noted by others, seem to reflect the substandard dietary ratings of this racial group which is generally credited with a high predisposition to pre-eclampsia and eclampsia. Too, it seems significant that in the white and Negro women in whom toxemia occurred, larger percentages of hemoglobin levels were below 10 and 12 Gm. in the third trimester than in women in whom toxemia of pregnancy did not occur. The fact, however, that median concentrations in both racial groups with toxemia did not decline as perceptibly during the seventh to ninth months as in normal gestations suggests that blood volume increases in pre-eclampsia-eclampsia do not follow the pattern of uncomplicated gestation. Dieckmann³⁰ showed that during the height of pre-eclampsia and eclampsia hemoconcentration occurs, followed by dilution with clinical improvement. This may, in part, account for the high incidences of low concentrations (below 12 and 10 Gm. levels) for both white and Negro women postpartum, after recovery from toxemia.

In summary, although low hemoglobin levels do not necessarily imply clinical evidence of nutritional deficiency, the close association of toxemia with low socioeconomic status, substandard diet, and anemia appears to be more than circumstantial.

Total Serum Protein.—Serum protein levels below 6 Gm. per 100 ml. generally are acknowledged as evidence of hypoalbuminemia. Fig. 1 indicates the medians and ranges for total serum protein concentrations among white and Negro women during uncomplicated pregnancies. The downward trends in concentration, with the curve for white women paralleling the curve for Negroes at consistently lower median concentrations portrays the usual effect of progressive hemodilution.

Table II gives the median concentrations of serum protein in white and Negro women with acute toxemias during the last trimester and the puerperium in comparison with concentrations at the same intervals in women whose pregnancies were uncomplicated. The table also presents the percentages of serum protein determinations below 6.0 Gm. per 100 ml., the level considered suggestive of protein deficiency.

TABLE II. SERUM PROTEIN LEVELS DURING UNCOMPLICATED PREGNANCIES AND PREGNANCIES COMPLICATED BY PRE-ECLAMPSIA AND ECLAMPSIA (GM. PER 100 ML. SERUM)

	WHITE	WOMEN	NEGRO	WOMEN
	NORMAL	TOXEMIA	NORMAL	TOXEMIA
Seventh Month.—				
Samples	81	6	97	.17
Median	6.06	6.13	. 6.24	6.45
Per cent below 6 Gm.	43	17	25	24
Eighth Month.—				
Samples	128	13	166	30
Median	5.98	5.94	6.24	6.17
Per cent below 6 Gm.	52	62	26	33
Ninth Month.—				
Samples	208	22	193	. 36
Median	6.00	5.64	6.23	6.24
Per cent below 6 Gm.	50	73	30	25
Post Partum.—				
Samples	142	18	187	25
Median	5.83	5.90	6.29	5.90
Per cent below 6 Gm.	62	56	30	56

A slight downward trend in median serum protein concentrations is evident for both racial groups with toxemia. As with groups of women whose pregnancies were uncomplicated, the Negro women with toxemias had consistently higher median levels than those of the white women. During the seventh month and post partum more white women whose pregnancies were uncomplicated had concentrations below the 6.0 Gm. level than the number of white women with pre-eclampsia and eclampsia whose serum protein levels were below that level. For Negro women, larger percentages of low levels of serum protein were found among those whose pregnancies were uncomplicated only during the eighth month of gestation.

As with hemoglobin, falling concentrations of total protein must be interpreted with caution since they may reflect blood volume increases rather than diminution in the total amount of protein available to the maternal organism. Moreover, electrophoretic studies^{31, 32} demonstrated that concentrations of several globulin components of plasma (alpha, beta, fibrinogen) increase progressively during normal gestation and that, for the most part, the increase of the same globulins is more abundant in pre-eclampsia-eclampsia, while gamma globulins and albumins decrease in concentration. Figs. 3 and 4 compare, at delivery and 6 to 12 weeks post partum electrophoretic patterns in uncomplicated pregnancy with those in pre-eclampsia and eclampsia. Because the different protein components of the plasma are variable in behavior and have widely divergent physiologic functions (as do various nutrients) determinations of total serum protein would seem to have limited value in assessing nutritional status in pregnancy. Scrimshaw and associates33, 34 believe that in human beings serum protein levels cannot be used to detect mild to moderate protein deficiency.

The differences in total serum protein concentrations between white and Negro women in this study may be of some significance, perhaps only genetic, since the latter had higher median levels in complicated and uncomplicated pregnancies. Other investigators35-37 also observed racial differences in serum protein concentrations. McGanity and co-workers6 noted significantly higher mean levels of serum protein in white women prior to recognition of toxemia symptoms. This observation may again reflect the results of hemoconcentration during the toxemia phase, just as the postpartum hypoproteinemia may result in part from hemodilution during the recovery period. Our electrophoretic studies,³² however, showed that even after albumins had been restored to essentially normal values, distortion of the globulin pattern persisted as late as 12 weeks post partum.

In summary, total serum protein determinations do not appear to provide a reliable criterion of nutritional state as a factor in the production of toxemia of pregnancy. Racial characteristics, blood volume fluctuations, and changing concentrations of the globulin components present a picture so variable that

it precludes interpretations of nutritional status.

Maternal Serum Vitamin C.—The constant necessity for ascorbic acid in the diet of human beings has been recognized for a long time, but only in recent years have attempts been made to establish requirements based on actual needs. Values of 0.2 to 0.6 mg. vitamin C per 100 ml. serum are generally regarded as the lowest compatible with health. This vitamin is considered an important regulatory factor in normal cell function, tissue growth, maintenance, and repair. Although the exact functions of this nutrient are not fully understood, it does play an important part in all growth processes and is abundant in active and growing tissues. High concentrations are found in the placental villi and in the adrenal glands during pregnancy.

In Fig. 1, the medians and ranges for serum vitamin C concentrations in white and Negro women during uncomplicated gestation demonstrate by downward trends the physiologic increase in blood volume from hemodilution. The higher level of vitamin C in white than in Negro women is indicative primarily of current food intakes since long-term storage of this labile, water-soluble vitamin does not occur.

Table III gives the median concentrations of serum vitamin C in white and Negro women with acute toxemia during the last trimester of pregnancy and post partum in comparison with concentrations at the same intervals in women whose pregnancies were uncomplicated; the percentages of determinations below 0.2 and 0.6 mg. vitamin C per 100 ml. serum also are given.

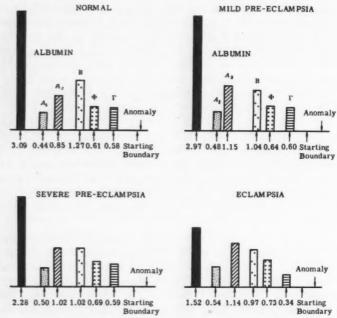


Fig. 3.—Averages for maternal plasma proteins at delivery, in normal pregnancy, in mild and severe pre-eclampsia, and in eclampsia. (From Mack. 22)

A distinct racial difference is apparent from the greater prevalence of low levels of serum vitamin C among Negro women, whether their pregnancies were normal or toxemic. A slight downward trend in median concentration from the seventh month to the puerperium seems apparent for Negro women whose pregnancies were normal and in toxemia. In the seventh and ninth months more determinations for Negro women whose pregnancies were normal were below the critical level of 0.2 mg. per 100 ml. Other marked differences were not found between concentrations in the sera of Negro women with or without toxemias.

For white women, very low median levels for normal pregnancies and toxemias were found only postpartum, with a greater number of determinations for white women who had pre-eclampsia and eclampsia below 0.6 mg. per 100 ml. Again, racial differences in the pre-eclampsia-eclampsia group merely suggest differences in eating habits rather than the effects of pregnancy or of its complications. Lund and Kimble, 38 also, did not find a decrease in plasma concentrations of ascorbic acid attributable to toxemia. The observation that the highest concentrations of vitamin C occurred in white women whose economic status and dietary ratings were highest may be significant. The lowered concentrations post partum may reflect decreased food intakes

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and increased vitamin C demands for wound healing following delivery, as well as the results of blood volume readjustment. Darby and his collaborators showed especially low ascorbic acid values in lactating women. In our patients, low levels (below 0.2 and 0.6 mg.) occurred with equal frequency in women of both races before delivery regardless of whether toxemia occurred in pregnancy; post partum, low levels seemed to be more prevalent among the women of both racial groups who had had toxemia.

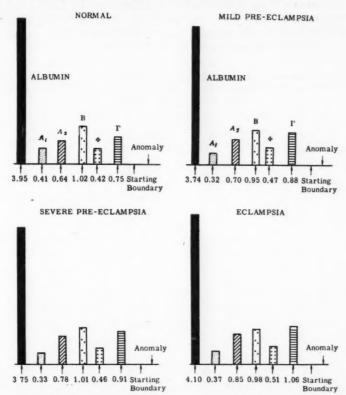


Fig. 4.—Averages for maternal plasma proteins 6 to 12 weeks post partum, after normal pregnancy, after mild and severe pre-eclampsia, and after eclampsia. (From Mack. 32)

Since vitamin C and proteins are involved in the pituitary-adrenal metabolic mechanisms of adaptation, it is conceivable that suboptimal vitamin C nutriture might be involved as a conditioning factor for toxemia under conditions of acute stress. A resemblance between the biochemical alterations of pre-eclampsia and eclampsia and those resulting from the hormonal imbalances observed in stress phenomena has been suggested.³⁹ This study provides no evidence suggesting a direct relationship between deficient vitamin C nutriture and the incidence of toxemia except that both seem to be more prevalent among women of low socioeconomic status.

Serum Vitamin A.—Vitamin A and its precursors, the carotenoids, are essential for growth and the preservation of health. They have special roles in the formation of epithelial cells and the maintenance of their integrity, in the shaping and molding of bone, in the formation of teeth, and in the visual cycle. Ranges of 30 to 70 μ g vitamin A are generally considered compatible with

health.

Fig. 2 shows the medians and ranges for serum vitamin A concentrations in white and Negro women during normal gestations. For women of both

races upward trends in early pregnancy were followed by a leveling off after the sixth month and lowered values post partum; the median level for Negroes after the sixth month was consistently lower than that for white women.

Most investigators consider 20 µg vitamin A per 100 ml. serum to be the lower limit of normalcy. Since the body can store vitamin A, especially in the liver, the effects of restricted intake may not readily become apparent in adult human beings. Disparity between white and Negro blood levels, also shown by Byrn and Eastman,⁴⁰ doubtless reflects differences in food intake and eating habits. Dietary evaluations for our patients corroborated serum vitamin A findings and quite consistently showed that inferior economic status was reflected in low serum levels for both white and Negro women.

TABLE III. SERUM VITAMIN C LEVELS DURING UNCOMPLICATED NORMAL PREGNANCIES AND PREGNANCIES COMPLICATED BY PRE-ECLAMPSIA AND ECLAMPSIA (MG. PER 100 ML, SERUM)

	WHITE	WOMEN	NEGRO	WOMEN
	NORMAL	TOXEMIA	NORMAL	TOXEMIA
Seventh Month				
Samples	78	6	92	17
Median	1.3	1.2	0.6	0.9
Per cent below				
0.2 mg.	0	0	8	0
0.6 mg.	9	33	51	41
Eighth Month.—				
Samples	128	12	158	31
Median Per cent below	1.2	1.2	0.6	0.6
0.2 mg.	2	0	5	6
0.6 mg.	18	17	52	52
Ninth Month.				
Samples	198	20	178	35
Median	1.2	1.1	0.6	0.6
Per cent below				
0.2 mg.	2	3	6	0
0.6 mg.	18	20	48	46
Post Partum.—				
Samples	138	17	181	25
Median	0.6	0.4	0.4	0.4
Per cent below				
0.2 mg.	10	24	14	20
0.6 mg.	53	88	. 66	68

Table IV gives the median concentration of serum vitamin A in white and Negro women with pre-eclampsia and eclampsia during the last trimester and post partum in comparison with concentrations at the same intervals in women whose gestations were uncomplicated. The table also lists the percentages of determinations below 20 μ g and 30 μ g per 100 ml. serum for both groups.

Median levels for white women were quite consistently higher than those for Negro women, both in normal and in toxemic pregnancies. During the seventh and eighth months white pre-eclamptic and eclamptic patients had higher median concentrations than did white women whose gestations were normal; in the ninth month the median levels were equal; post partum the white women whose pregnancies were normal showed somewhat higher median concentrations. Negro women during normal pregnancies had median concentrations prior to delivery approximately the same as those of Negro women with toxemia; post partum the median level for Negro women who had had normal pregnancies was somewhat higher than in cases of toxemia.

TABLE IV. SERUM VITAMIN A LEVELS DURING UNCOMPLICATED PREGNANCIES AND PREGNANCIES COMPLICATED WITH PRE-ECLAMPSIA AND ECLAMPSIA (µG. PER 100 ML. SERUM)

	WHITE	WOMEN	NEGRO	WOMEN
	NORMAL	TOXEMIA .	NORMAL	TOXEMIA
Seventh Month.—				
Samples	80	6	88	16
Median	42	58	30	30
Per cent below				
20 μg	2	0	22	19
30 µg	21	33	49	50
Eighth Month.—				
Samples	127	13	148	27
Median	36	51	31	29
Per cent below				
20 μg	9	23	18	11
30 μg	32	31	46	52
Ninth Month.—				
Samples	198	19	176	35
Median	39	38	34	34
Per cent below				
20 μg	10	16	18	26
30 μg	25	26	41	40
Post Partum.—				
Samples	133	15	163	26
Median	44	31	39	32
Per cent below				
20 μg	7	20	7	12
30 µg	16	47	23	46

In general, more white toxemic subjects had low levels of vitamin A concentration than did women with uncomplicated gestations. For Negro women, this index of deficiency in nutrition was notable only during the postpartum period.

Serum Carotenoids.—Ranges of 100 to 300 µg of carotene are generally considered compatible and less than 60 µg of carotene per 100 ml. serum is judged to be incompatible with health and well-being. Fig. 2 contains the medians and ranges for white and Negro women during normal gestations. An upward trend, leveling after the sixth month and a downward trend from the ninth month to the puerperium are apparent for both racial groups; slightly higher median levels were observed for white than for Negro subjects. Statistically significant relationships were noted between carotenoids and vitamin A concentrations for white and Negro women at all stages of pregnancy and early post partum. Serum carotenoids and vitamin C were positively correlated for all groups studied.

Table V gives the median concentrations of serum carotenoids in white and Negro women with pre-eclampsia and eclampsia in the last trimester of pregnancy and post partum in comparison with levels at the same intervals in women whose pregnancies were uncomplicated. The table itemizes the percentages of determinations below the levels of 60 and 100 µg per 100 ml. for both groups.

Median levels for white pre-eclamptic and eclamptic patients were consistently higher than those for women whose pregnancies were normal; in Negroes the opposite was true. Low levels of serum carotenoids were more prevalent at delivery and post partum among white women with toxemia; comparisons for Negro women with and without toxemia did not show this trend.

Table V. Serum Carotenoid Levels During Uncomplicated Pregnancies and Pregnancies Complicated by Pre-eclampsia and Eclampsia (µg. per 100 ml. serum)

	WHITE	WOMEN	NEGRO	WOMEN
	NORMAL	TOXEMIA	NORMAL	TOXEMIA
Seventh Month.—				
Samples	81	6	90	16
Median	175	190	167	140
Per cent below				
60 μg	2	0	0	0
100 μg	4	0	6	0
Eighth Month				
Samples	127	13	148	29
Median	178	210	166	157
Per cent below				
60 μg	2	0	1	0
100 μg	8	0	5	7
Ninth Month				
Samples	204	20	181	35
Median	163	230	168	158
Per cent below				
60 μg	0.5	5	0.5	0
100 μg	9	15	14	8
Post Partum.—				
Samples	135	16	168	27
Median	138	150	144	118
Per cent below				
60 µg	- 3	12	2	0
100 μg	23	25	14	33

In summary, deficient levels of vitamin A in the serum were prevalent among both white and Negro women with toxemia of pregnancy and reflected the inferior nutritional status of these women. A similar situation was not found for blood levels of serum carotenoids.

Serum Alkaline Phosphatase.—Alkaline phosphatase enzymes are widely distributed in the organs and tissues of the body, occurring in higher concentrations in bone and ossifying cartilage. Serum alkaline phosphatase activity is related to calcium and vitamin D nutriture and has been used as a standard for judging vitamin D deficiency in nutritional status studies of population groups. The average alkaline phosphatase concentration of nonpregnant white women in our investigations was 1.36 nitrophenol units.

TABLE VI. SERUM CAROTENOID LEVELS DURING UNCOMPLICATED PREGNANCIES AND PREGNANCIES COMPLICATED BY PRE-ECLAMPSIA AND ECLAMPSIA (NITROPHENOL UNITS)

	WHITE	WOMEN	 NEGRO 	WOMEN
	NORMAL	TOXEMIA	NORMAL	TOXEMIA
Seventh Month.—				
Samples Median	83 1.96	$\frac{6}{2.00}$	$\frac{95}{2.06}$	$\frac{17}{2.31}$
Eighth Month.—				
Samples Median	$\frac{131}{2.81}$	$\frac{13}{3.25}$	$\begin{array}{c} 156 \\ 2.68 \end{array}$	28 2.92
Ninth Month.—				
Samples Median	$\begin{array}{c} 205 \\ 3.49 \end{array}$	$\frac{22}{4.17}$	189 3.80	37 3.38
Post Partum.—				
Samples Median	142 3.33	18 3.90	180 3.43	27 3.54

Fig. 2 shows the steadily increasing concentrations of alkaline phosphatase in the serum of white and Negro women whose uneventful gestations culminated in delivery of single, healthy infants at term. The upward trend through the ninth month was followed by almost identical decreases in the early puerperium.

Similar upward trends in pre-eclampsia and eclampsia, with probably insignificant variations for racial groups, is shown by the median values for normal and toxemic pregnancies given in Table VI.

Nothing significant in the data presented suggests a relationship between this enzymatic activity and the occurrence of the true toxemias of pregnancy.

Conclusions

Strong circumstantial evidence supports the general belief that malnutrition plays an important part in susceptibility to pre-eclampsia and eclampsia. Surprisingly, it is not easy with methods presently available to find biochemical evidence completely to support this view. The foregoing report of attempts to assess nutritional involvement in subjects who developed toxemia, using clinical, dietary, and microchemical procedures, emphasizes the complexities of the problem. Mass surveys of this type must recognize for the population group observed the many different, variable influences, such as race, socioeconomic status, and the stability of food sources. Better standardization of methods is necessary and additional techniques must be devised to assay the many other nutrients known to be essential to health.

From the mass of data, frequently contradictory, bearing on the relationship between nutritional state and susceptibility to toxemia of pregnancy, at least one general conclusion is emerging: among the several nutritional factors found to be essential for growth and reproduction, no one factor has been shown as yet to play a decisive and specific role in protecting against eclampsia. Knowledge that normal gestation may occur with suboptimal blood levels of essential constituents makes it clear that the normal gravida is able to compensate, at least to a high degree, for the avid demands of the fetus upon her food intakes and stores. The fact that some mothers escape toxemia, even though their blood levels of nutrients show them to be on the brink of starvation, does not eliminate malnutrition as a factor in pre-eclampsia and Rather, this emphasizes that survey methods must be improved and expanded, since not one but perhaps many longstanding nutritional deficits may be involved in the "hidden hunger," and the resultant conditional malnutrition may constitute a predisposing factor to the occurrence of toxemia.

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Discussion

DR. ROBERT A. ROSS, Chapel Hill, N. C .- The essayists by pursuing a careful study of certain dietary factors in a selected group of patients have made further progress in solving the riddle of the late toxemias of pregnancy. They evaluate conflicting data and immediately recognize the difficulty in matching clinical impressions and findings with precise laboratory methods. The number and division of their studied patients are adequate for deductions and impressions. Their criteria for "toxemia" are sound and generally accepted. The dietary habits are always difficult to determine. The tests for determining the "nutritional status" seem to be chosen wisely and should give

All are familiar with the vagaries of hemoglobin levels during pregnancy. These investigations found significant lowering, which, associated with low socioeconomic status, substandard diet, and the increased occurrence of toxemia, led them to believe that it was more than coincidental.

Total serum protein did not provide a reliable criterion, due, they think, to racial characteristics, blood volume fluctuations, and changing concentration of globulin components. We have found serum protein determinations to be consistently lower in the toxemia patients, as well as alterations of albumin-globulin ratio. We believe that the proteins in the diet should be listed qualitatively, as well as quantitatively.

In studying serum vitamin C values the authors recognize that such findings chiefly reflect the current dietary habits. By suggesting a relationship of vitamin C and proteins with the pituitary-adrenal function as a factor in the "stress phenomenon," they are adding another imponderable.

As anticipated, the vitamin A concentrations were more revealing and a lower level was noted in the toxemic patient. No change was noted in blood levels of serum carotenoids.

Serum alkaline phosphatase activity is related to calcium and vitamin D utilization and should be useful in such studies. However, there was no significant alteration in this enzymatic activity.

The authors apparently believe that there is some relationship between nutritional status and the incidence of the toxemias of pregnancy. This discussant believes this strongly. As the population shifts, other observers will be confronted with the medically inarticulate and with the increased incidence of the toxemias of pregnancy.

DR. R. L. NEWMAN, Kansas City, Kan.—The importance and extent of the work performed by Dr. Mack and his associates in Detroit during the past eight years are familiar to anyone who has read their publications. This is their first attempt to compare abnormalities of gestation occurring in their study group with their carefully established

The authors caution in their paper that "the frequencies of normal and complicated pregnancies and toxemia portray the characteristics of one study group and do not present valid statistical evidence of the relationships of either race or living standards to the development of pre-eclampsia and eclampsia in a cosmopolitan community." Despite that statement, it was interesting to study their figures from that viewpoint.

Fifty-four patients developed pre-eclampsia or eclampsia. It is not clear from the paper whether 6 of these patients (5 with eclampsia and 1 with pre-eclampsia, "previously reported") were included in the original study group or not.

NEGRO PATIENTS

33 of 54 patients with pre-eclampsia-eclampsia = 61% 686 of 1,064 patients in study

Thirty-three of the 54, or 61 per cent, were Negroes. However, 686, or 64 per cent, of the 1,064 patients in the original study group were Negroes. Thus, if the figure of 54 toxemic patients can be used, 33 of 686 Negro patients, or 4.8 per cent, developed toxemia while 21 of 378 white patients, or 5.5 per cent, developed the disease. If the group with eclampsia is eliminated, then 31 of 686 Negro patients, or 4.5 per cent, as compared with 18 of 378 white patients, or 4.8 per cent, developed pre-eclampsia.

54 PATIENTS WITH PRE-ECLAMPSIA OR ECLAMPSIA

21 of 378 white patients = 5.5%

33 of 686 Negro patients = 4.8%

49 PATIENTS WITH PRE-ECLAMPSIA

18 of 378 white patients = 4.8%31 of 686 Negro patients =4.5% The original study series used by Dr. Mack and his associates consisted of three groups: Group A, made up of 109 white and 544 Negro patients that might be called the indigent group; Group B of moderate means consisting of 33 white and 131 Negro patients; and Group C of 230 white patients with something more than moderate means.

DISTRIBUTION OF PATIENTS ACCORDING TO ECONOMIC STATUS

A	(LOW	INCOME)
	109	White
	544	Negro

В	(MO	DERATE)
	33	White
	131	Negro

C (MORE THAN MODERATE) 230 White

PRE-ECLAMPSIA-ECLAMPSIA

10 of 109 white patients in Group A=9.1%27 of 544 Negro patients in Group A=4.9%

11 of 263 white patients in Groups B & C = 4.1% 6 of 131 Negro patients in Groups B & C = 4.6%

Twenty-seven of 544, or 4.9 per cent, of the Negro patients in Group A developed toxemia, while 10 of 109 white patients, or 9.1 per cent, in this group developed the disease. Six of 131 Negro patients in Groups B and C, or 4.6 per cent, developed the lesion as compared with 11 of 263 white patients, or 4.1 per cent.

These figures would seem to argue against any marked racial predilection for the Negroes in this particular study group of patients in the development of toxemia.

Dr. Mack and his co-workers have demonstrated in their studies a preponderance of inadequate diet in the Negroes. Consequently, one cannot help but wonder as to the importance of the dietary factor in the development of toxemia, again as it applies to this particular study group.

The relatively high incidence of toxemia in the indigent white patients produces speculation as to the possibility of some other factor occurring in the presence of a low socioeconomic and dietary environment, perhaps even the factor of "stress" mentioned by the authors.

These comments, of course, do not in any way affect the importance of this paper. Here are the results of a real scientific effort to investigate a relatively unknown field, that of human nutrition, and compare the findings in complications of pregnancy with well-established normals. It is rather discouraging that more clear-cut trends could not be established with their battery of biochemical determinations in pre-eclampsia and eclampsia. It is from such efforts as this, however, that our future knowledge accumulates.

DR. N. LOUROS, Athens, Greece.—If I avail myself of the opportunity to discuss Dr. Mack's paper, which I have greatly appreciated, it is because I would like to report to you conditions in Greece concerning late toxemia.

We have exceptionally little of it and we believe it is due to the reduced quantity of protein, animal fat, and salt consumed by our population. This concept is supported by the fact that eclampsia almost disappeared during the German occupation of Greece when our calorie intake was about 450 a day. I know this is contrary to the contention that eclampsia is due to a hypoproteinemia and also to the satisfactory therapeutic results obtained or claimed with high-protein feeding during pregnancy. But we cannot change the results of our experience.

I also would like to point out the well-known relationship between the outbreak of eclampsia and weather conditions. Nothing definite has been found until recently in research on conditions inside the atmosphere. Collaborating with the meteorological department of the Royal Greek Air Force, we have now found that in every outbreak of eclampsia mentioned in our records there was a preceding change in the predominance of the aerial front above the atmosphere. This also induces a change in the distribution of the electrons inside the atmosphere. Thus an important impulse is imposed by the electrons on the vegetative nervous system, and the vasomotor changes leading to eclampsia can thereby be explained.

In geographic medicine the explanation of contrary findings calls for a close collaboration between scientists of various countries.

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DR. MACK (Closing).—Our study contains a number of considerations which will appear in the published manuscript which I could not give in this abbreviated presentation. I recognize from Dr. Newman's discussion that some of these were not made sufficiently clear.

I agree that it is confusing when we presented the backgrounds of our original study group and then confined our consideration to the subjects with toxemia. We tried to make it clear that we could not draw statistical inferences as to the incidence of toxemia in the three groups because they did not represent random samples of the population. We have attempted merely to present the biochemical data pertaining to nutrition from this small group of subjects who developed toxemia and to compare them to the trends we observed in women whose pregnancies were entirely normal. The results show that the differences were often minimal. I must confess that the lack of sharply defined differences was somewhat disappointing to me because I am still convinced that there is something in the nutritional background which contributes to the incidence of toxemia. We see this in our daily practices with clinic patients as compared to experiences in private practice.

Dr. Louros also shows how confusing the whole story is by pointing out that the incidence of toxemia in Greece seems to lessen as the diet appears to grow worse. This again emphasizes the need for more intensive mass surveys of this type and shows that we must take into account the environmental, socioeconomic, and racial factors. We tried to point this out in our paper.

ETIOLOGY OF PRE-ECLAMPSIA-ECLAMPSIA

VI. Sodium, Potassium, Nitrogen, and Water Content of Muscle and Skin in Pre-eclampsia*†

WILLIAM J. DIECKMANN, S.B., M.D., AND R. E. POTTINGER, S.B., S.M., CHICAGO, ILL.

(From the Department of Obstetrics and Gynecology of the University of Chicago and the Chicago Lying-in Hospital)

A MONG the many theories which have been proposed to explain the cause of pre-eclampsia-eclampsia are two which recur periodically; water intoxication and "salt" poisoning. They are opposite in that in the former there is an excess of water and in the latter an excess of electrolyte. Several reports based on a small number of cases, mostly autopsy material, state that in eclampsia there is a tremendous increase in muscle sodium. As a part of our study of the water and electrolyte metabolism in pre-eclampsia-eclampsia, pieces of the rectus muscle and abdominal skin were obtained from patients with pre-eclampsia, hypertensive disease, normal pregnancy, and from non-pregnant women, and analyzed for sodium, potassium, nitrogen, and water. Many of these patients also had water and electrolyte changes determined for the extra- and intracellular fluid compartments² as well as Na²² space and turnover.

Twenty years ago it was believed that the sodium ion was limited to the extracellular fluid where each liter of fluid contained approximately 150 meq. of sodium ions. During the past 15 years studies on animals and humans have shown beyond question that sodium can enter muscle and other cells in the body. The increase of intracellular sodium, if great enough, causes marked signs and symptoms, depending upon the organ involved. When sodium and potassium shift, other cations such as magnesium and calcium and the various anions also shift; thus the function of organs will be seriously impaired if the change is large enough.¹⁴

Obstetrical textbooks and the monographs by Halben and Seitz⁵ and by Hinselmann⁶ give no data about sodium and potassium concentration within the body cells.

Rossenbeck¹⁰ in 1931 reported the electrolyte analyses of the tissues obtained at autopsy from one patient who died from eclampsia and a second pregnant patient who died during an epileptic attack. He stated that the

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^{*}Supported in part by the Chicago Lying-in Hospital Fiftieth Anniversary Fund for Eclampsia.

[†]Presented at the Sixty-sixth Annual Meeting of the American Association of Obstetricians and Gynecologists, Hot Springs, Va., Sept. 8 to 10, 1955.

muscle sodium and chloride ion concentrations were increased in normal pregnancy and that in the eclamptic patient there was a marked increase in the sodium content and a marked decrease in the potassium concentration in the muscle. The potassium content in the brain was slightly decreased.

Parviainen and associates⁹ in 1950 reported the sodium and potassium concentration in tissues obtained after death in a patient with pre-eclampsia who died from a cerebral hemorrhage. They reported a higher sodium concentration and an increase in the Na:K ratio in pre-eclampsia over that in the control case. They thought that there was a causal relation.

Nordenstrahl^s in 1952 reported electrolyte studies of tissues obtained after death from 4 patients with eclampsia and 8 other pregnant women. Potassium was retained more extensively in toxemic patients than in normal pregnant women. The potassium concentration in the serum water was probably somewhat higher in cases of toxemia. The potassium concentration in the erythrocyte cell water was the same. The potassium concentration in voluntary muscle and brain tissue was unchanged. There was no difference between the sodium concentrations in the erythrocyte cell water. The retained potassium in cases of toxemia was recovered in the brain and voluntary muscle; the edema in these organs was partially intracellular. The edema in the liver and kidney was chiefly interstitial. Nordenstrahl did not determine the sodium in the voluntary muscle.

There have been a number of studies of the electrolyte content of human and animal voluntary muscle in nonpregnant normal and abnormal, including edematous, individuals. Talso and co-workers¹² in 1953 reviewed the more recent literature and analyzed skeletal muscle obtained at operation or by biopsy from 8 patients with cardiac edema and 8 patients who had been edematous but who were partially or completely free of edema. They found an increase in total tissue water representing an increase in both extra- and intracellular water content. The sodium content of the edematous tissues was increased over the control values. They stated that various reports suggested a universal decrease in intracellular electrolyte content in heart failure and that although their data fitted this current concept, "they are open to criticism."

Grollman⁴ in 1954 studied the water and electrolyte content of tissues from rats with hypertension and concluded that the values in the hypertensive animals did not differ from those obtained in a series of control normotensive animals. He concluded that the changes in water and electrolyte content of the tissues observed by previous workers are not essential characteristics of the hypertensive state, but are to be attributed rather to renal disturbances.

Cannon and co-workers¹ studied sodium and potassium ion concentration in the tissues of protein-depleted rats. They concluded that sodium chloride in the diet becomes quickly and lethally toxic in these animals in the presence of severe potassium depletion: "Under conditions of potassium depletion, the excessive intracellular accumulation of sodium and possibly of hydrogen ions

as well, particularly in cardiac muscle, may so injure intracellular enzyme activity as to initiate processes of necrobiosis and the resulting coagulating necrosis."

All evidence at hand indicates that an excess or depletion of sodium, potassium, chloride, water, and undoubtedly of other ions found both extra- and intracellularly will result in clinical manifestations if the changes are of sufficient magnitude, and even death may result.

Abnormally low and high serum potassium and sodium concentrations have been reported and typical syndromes have been described for each of the four conditions.^{7, 11, 13} Hypernatremia is just becoming recognized as a elinical entity. Since comparatively large amounts of sodium ions are in the interstitial fluids, less in bones, and still less in cells, it is obvious that significant prolonged changes in the serum concentration must be associated with changes in these compartments. Potassium is primarily intracellular but it obeys the same chemical laws that affect sodium.

Method

We obtained biopsies of the skin and rectus muscle at cesarean section. In a few cases skin and gastrocnemius muscle were obtained. If local anesthesia was used the procaine solution was injected intradermally and only muscle was obtained. All of the tissues were obtained at delivery. There has been no opportunity for comparison of anteand postpartum values in the same patient. Tissues from nonpregnant women, 20 to 40 years of age, were obtained at laparotomy of gynecological patients. The samples were immediately cleaned of blood and visible fat was removed. They were placed in weighing bottles with an outside ground cap and weighed. The cap was removed, placed with the bottle in an oven at a temperature of 110° C. until the dry weight became constant. After the water content was obtained, the tissues were analyzed. The tissue was extracted with ether once and dried again to constant weight. It was then transferred to a micro-Kjeldahl flask and the ether extract was also added. One milliliter of concentrated sulfuric acid was added to the weighing bottle which was replaced in the oven until the remaining powder was in solution and it, too, was transferred to the Kjeldahl flask with the initial tissue. This procedure was repeated one more time to remove completely all of the tissue from the weighing bottle. Thirty per cent hydrogen peroxide was used in small amounts to aid in the digestion. The clear solution was transferred to a 25 ml. volumetric flask and when cool was made up to volume. Nitrogen and phosphorus were determined in aliquots. Ten milliliters was evaporated to dryness in Vycor crucibles. The last part was accomplished by heating over an open Bunsen burner which completely removed all of the sulfuric acid. Sodium and potassium were extracted from the ash material as sulfates and the extracts made up to 25 ml. Portions of this solution were used for the determination of sodium and potassium with the Beckman gas-oxygen flame photometer. All analyses were determined each day in comparison with sodium and potassium standards. The empty weighing bottles were reweighed after cleaning and drying and their weights were found to remain constant. Duplicate analyses were made whenever sufficient tissue was obtained.

Chloride was determined in only a limited number of tissues because more tissue was required and the chemical work was doubled. Even though we calculated chloride space it did not not add to our knowledge of an existing cellular abnormality. Phosphorus likewise was determined, but did not add to our knowledge.

The analytical data are calculated in terms of: (1) fat-free wet tissue; (2) fat-free dry tissue; and (3) tissue water.

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Illustration .-

If sodium content was 40 meq./kg. and water was 75 Gm. per cent in wet fat-free tissue,

In dry fat-free tissue the sodium = $100/25 \times 40 = 160$ meq./kg. In tissue water the sodium = $100/75 \times 40 = 53$ meq.

Comparisons were made between the tissues obtained from (1) nonpregnant and normal pregnant women; (2) normal pregnant and those with preeclampsia and hypertensive disease; and (3) patients with pre-eclampsia and hypertensive disease. Only differences which were statistically significant are discussed.

RECTUS MUSCLE

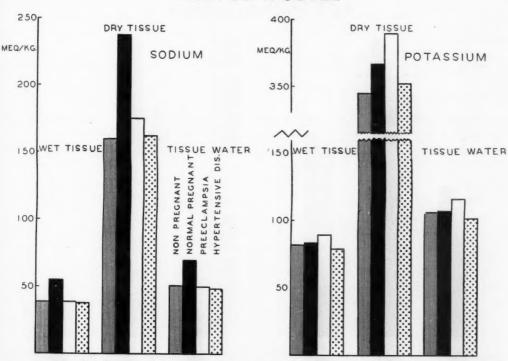


Fig. 1.—Shows muscle sodium and potassium content. Note increase of sodium in normal pregnancy, but essentially nonpregnancy sodium content in pre-eclampsia and hypertensive disease. Potassium is unchanged.

TABLE I. SODIUM, POTASSIUM, NITROGEN, AND WATER CONTENT OF SKIN AND RECTUS MUSCLE (MEAN VALUES FOR FAT-FREE WET TISSUE)

	SODI MEQ.		POTASS MEQ.		Na:K RATIO	NITRO GM.		WAT GM.	
	MUSCLE	SKIN	MUSCLE	SKIN	MUSCLE	MUSCLE	SKIN	MUSCLE	SKIN
Nonpregnant 9 patients	38	96	81	17	0.485	2.68	4.69	76.3	66.1
Normal pregnant 17 patients	54	111	83	20	0.665	2.90	3.62	77.2	73.8
Pre-eclampsia 20 patients	37	98	89	20	0.445	2.86	3.54	77.7	74.6
Hypertensive dis- ease 41 patients	37	96	79	17	0.502	2.86	4.16	77.5	72.5

Table I shows mean values for the constituents studied. The range in the tissues was not excessive. Four separate studies beginning in 1949 have been made and the range and mean values from the second, third, and fourth series confirm the initial analysis; only the first three are included in this report.

Studies in progress enable us to obtain a control piece of skin and rectus muscle and then inject Na²² and/or 1,000 ml. of a 2.5 per cent solution of sodium chloride and obtain later specimens. Within 30 minutes after such a test load of sodium chloride solution, there is a marked increase in muscle sodium and a lesser decrease in potassium; but the total meq. of these cations increased. The opposite rectus muscle showed a similar change. Thus, there is a transient hyperosmolarity of the rectus muscle and presumably of other cells. Further observations will indicate the duration of this change.

ABDOMINAL SKIN

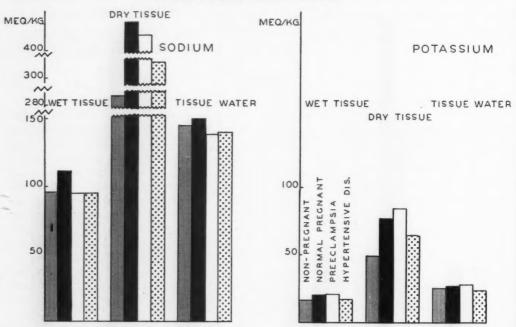


Fig. 2.—Shows skin sodium and potassium content. Note increased content of sodium in the wet tissue over that in normal pregnancy. In dry tissue it is increased above that of nonpregnancy and hypertensive disease. Tissue water differences are significant for normal pregnancy and hypertensive disease. Potassium is unchanged.

It was obviously impractical to obtain many tissues from the abdominal wall and leg, but in the few cases where such tissues were obtained from both sites or only from the leg, the concentrations of sodium and potassium are similar to those of the rectus muscle. The significant changes are shown in Figs. 1, 2, and 3.

Fig. 1 shows that there is an increase (medium significance) in the sodium content of the wet and dry rectus muscle and tissue water in normal pregnancy. In pre-eclampsia and hypertensive disease the values for sodium in wet and dry muscle and in tissue water are *lower* (medium significance) than in normal pregnancy. In fact, the values are the same as for the nonpregnant.

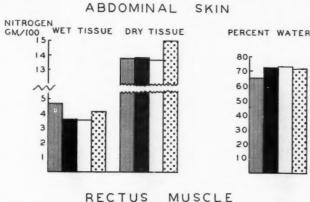
Potassium concentrations in rectus muscle and tissue water show no significant changes between nonpregnancy and normal pregnancy, and between normal pregnancy and pre-eclampsia and hypertensive disease.

Fig. 2 shows the increase (low significance) in sodium in the wet skin in normal pregnancy. In the dry skin there is an increase (very high significance) in sodium in normal pregnancy. In pre-eclampsia and hypertensive disease sodium in wet tissue is lower than in normal pregnancy. In preeclampsia it is increased above that from hypertensive disease. The sodium in the tissue water is decreased in pre-eclampsia and hypertensive disease.

Potassium in normal pregnancy is unchanged in wet tissue but increased on dry skin basis. In pre-eclampsia and hypertensive disease it shows no

Fig. 3 shows that the water in the skin from patients in normal pregnancy, pre-eclampsia, and hypertensive disease is increased.

SKIN



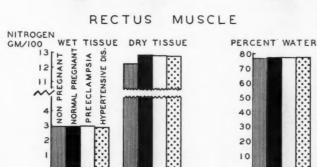


Fig. 3.—Lower graphs show no change in rectus muscle nitrogen and water.

Upper graphs show water content of skin is increased by pregnancy. Nitrogen content is less in normal pregnancy. It is increased in hypertensive disease above that from normal pregnancy and pre-eclampsia.

The nitrogen is decreased (high significance) in wet skin in normal pregnant patients (Fig. 3). In patients with hypertensive disease it is greater (medium significance) than in normal pregnant or pre-eclamptic patients.

There is no significant change in the water content of the rectus muscle in any of the four groups of patients. The nitrogen content shows no change.

Table I shows that the Na:K ratio is increased in muscle from normal pregnant patients, but is decreased in patients with pre-eclampsia (high significance) and hypertensive disease (medium significance) to nonpregnancy There is a significant difference between the Na:K ratio in normal pregnant patients and in pre-eclamptic and hypertensive patients.

The Na:K ratio in skin shows no real difference.

Table II contains serum and tissue values for representative patients. Cases 6 and 7 each had abnormally low serum sodium and chloride concentra-

Table II. Values for Tissue and Serum Electrolytes (Fat-Free Wet Tissue)

		SER	SERUM		MUS	MUSCLE			SKIN	N	
DIAGNOSIS AND CASE NUMBER	SODIUM (MEQ./	POTAS- SIUM (MEQ./ L.)	CHLORIDE (MEQ./ L.)	SODIUM (MEQ./ L.)	POTAS- SIUM (MEQ./ *	GEN (GM. %)	WATER (%)	SODIUM (MEQ./ L.)	POTAS- SIUM (MEQ./ L.)	GEN GEN (GM. %)	WATER (%)
Normal Nonpregnancy.											
		5.4	102	38	83	2.95	73.6	118	26	4.47	62.2
100	139	5.1	104	30	92	2.90	75.7	93	13	4.85	87.29
Normal Pregnancy-											
ಣ	135	4.7	102	56	85	2.85	74.7	130	20.5	3.72 *	73.2
4	137	5.1	101	53	92	2.90	79.5	98	17	3.14	76.4
Eclampsia.—											
10	138	6.0	105 (ante partum)	44	100	2.97					
	138	5.4	_								
9	114	5.1	-	32	75	2.38	80.7	75	11.9	4.14	73.7
	141	4.6	-								
7	117	3.9	98 (ante partum)	39	74	2.78	79.1	110	00	2.65	80.3
	117	5.1	-								
00	141	5.5		41	71	3.36	74.5 leg	91	16	4.58	72
Pre-eclampsia.—											
6	130	5.1	109	50	91		79.0 leg	108	31		78.25
10	133	5.5	104	90	101		79.8	110	16		74.8
11	136	5.6	105	34	94	2.89	79.5	26	19	3.05	78.5
Hypertensive Disease.—											
12	134	5.1	107	31	89	3.26	78.2	121	20	5.95	63.6
13	139	5.0	108	30	89	2.83	28	111	16.5	3.42	77.8
14	129	10.	103	44	62	3.10	92	98	26	4.44	70.3

tions, Case 6 from hypotonic body fluids due to a retention of some 13 L. of water and Case 7 from vomiting due to pyelonephritis and ileus. An attempt was made by intravenous injections of sodium lactate, saline, and plasma to correct the imbalance in Case 7 but this treatment presumably precipitated convulsions. Despite the sodium and chloride injections the serum values were still subnormal on discharge. The patient has had two subsequent normal pregnancies with normal serum electrolyte. Case 6 received no electrolytes for 5 days and then less than 12 meq. of sodium and chloride daily; at discharge the serum electrolyte values were normal (Table III).

TABLE III. BLOOD CHEMISTRY IN CASE 6

DAY	SERUM PROTEIN (GM. %)	Na (MEQ.)	cl (MEQ.)	K (MEQ.)	NPN (MG. %)
1	4.4	114	84	4.9	49
Delivery	3.4	107	81	4.5	
1	3.2	114	82	5.2	39
2	3.6	120	81.5	5.0	37
3	3.7	122	82	4.6	32
6	4.1	126	82	4.9	23
9	4.7	134	100	4.5	
12	5.4	138	101	4.6	
13	5.2	141	105	4.6	21
30	6.6	132	104	5.4	44

TABLE IV. CLINICAL COURSE OF CASE 6 IN FIRST HOSPITAL

DATE	BLOOD PRESSURE (MM. HG)	PROTEIN- URIA (GM. %)	TROSE 5% (ML.)	OUTPUT (ML.)	REMARKS
3/5	130/70	0				76 kg.
5/4	125/70	0				85 kg.
23	160/90	2+	•			90 kg.
24	170/100	++++	3,000	175		Convulsions 2, NPN 32 mg. %, X-ray shows 5 months' fetus no fetal heart tones
25	150/115	8.8	2,000	600 275 v	v*	
26	195/135	1.1	2,000	300 50 1	v	
27	180/120	0.7	2,000	300 60 v	v	NPN 56 mg. %
28	180/90		1,000	180 170	v	
29	190/120	7.1	2,000	1,100		
30	190/130	7.5	2,000	1,100		
31	160/105	12.0	2,000	600		NPN 54 mg. %
6/1			3,000	400		

kė 19,000+ Urine 4,860 Emesis 600 Balance 13,000+

*v = vomitus.

We wait for studies in progress to explain these various changes but they have clinical value. We have the case report of a patient who had been given adequate prenatal care, but at 37 weeks' gestation was found to have 2 plus edema, 1 plus proteinuria, and blood pressure of 180/130. She walked to the hospital. During the next 10 hours she was given sedatives and three injections of 1,000 ml. 5 per cent dextrose and thereafter had convulsions, coma, marked hypertension, an oliguria with bloody urine, and several hours later

TABLE V. CLINICAL COURSE OF CASE 6

	WEIGHT (KG.)	EDEMA	BLOOD	PROTEINURIA (GM./24 HR.)	INTAKE (ML.)	(ML.)	OUTPUT (ML.)	REMARKS
91.55	io.	‡	190/130	4.3	1,000	50%	200 135 119 50 v*	6:00 P.M. admitted to Lying-in Hospital. No fetal heart tones. Generalized edema. · Doughy skin, bloody urine
600	93.17 (ante partum) 89.62 (post partum)	++++	230/130	7.4	350	50%	300 60 v	Hysterotomy, 710 Gm, live fetus, 500 ml 12% dextran
00	88.13	+ + + +	180/95	7.9	200	30%	1,780	
36	86.52	++++	170/95	7.4	1,000	20% oral	1,110	Urine bloody
36	86.97	+++++	200/120	7.1	1,000	20% oral	1,390	
98	86.27	‡	155/100	6.8	1,000	10% oral	3,160	
34	.70	++++	170/140	3.8	3,335	oral	2,290	
35	85.20	+++	150/90	3.0	4,825	oral	6,300	
9	.4	‡	120/80		,			Discharged
03	9.	+	140/90	1.6				1
	ಲ್	0	115/70	1.1				

 $^*v = vomitus.$

died. In a period of about 10 hours she had 3,000 ml. of 5 per cent dextrose solution intravenously but excreted only 300 ml. of urine, a positive balance of 2,600+ ml. Obviously, with already abnormal extra- and intracellular fluid compartments, the additional 2,600 ml. of fluid (6 per cent of her total body water) undoubtedly had something to do with the sudden increase in severity of the pre-eclampsia and probably precipitated the convulsions. Autopsy showed marked edema of all tissues and an extensive hemorrhage over the frontal lobes. This patient walked to the doctor's office and to the hospital; she did not have fulminating eclampsia. She might have died with any type of treatment, but why give such a patient parenteral fluids of any type or concentration? Amniotomy or cesarean section under local anesthesia after proper observation for 12 to 24 hours might have resulted in a live mother and baby.

Case 6, a 34-year-old primigravida at term on Sept. 2, 1955, had similar treatment but survived. She was first seen by her family doctor on March 5, 1955. Because of hypertension, proteinuria, and edema he sent her to a hospital in Indiana on May 24. Between May 24 and 31 she was given 19 L. of 5 per cent dextrose intravenously, oral intake is unknown, and excreted 4,860 ml. of urine and 600 ml. of vomitus. Thus there was a positive balance of some 13 L. (Table IV). The senior author had been consulted by telephone on May 29, because of the oliguria, and had agreed to accept the case. She did not reach our hospital until late on June 1, with the findings and course as shown in Table V.

She was in coma for 48 hours, uncoordinated another 3 days, and unable to read for 7 days. Her temperature never exceeded 37.8° C., maximal pulse was 128 on the third hospital day, and maximum respiratory rate was 24; yet her condition was obviously critical.

Table III shows chemical data for Case 6 which were confusing; i.e., high hematocrit but low serum protein, sodium, and chloride concentration. We considered hemoconcentration³ and dehydration even though there was obvious marked edema and therefore followed the 200 ml. of 50 per cent dextrose solution with 1,000 ml. 10 per cent dextrose solution. The urinary response to the latter solution was minimal and convinced us that there was no tissue dehydration. We concluded that there was a severe oliguria presumably due to the pregnancy, with possibly a cortical necrosis of the kidney or lower nephron nephrosis; and that the pregnancy should be interrupted. The low serum sodium and chloride, had they occurred two years ago, would have been treated by us with parenteral NaCl solution. In view of our studies of the composition of the body fluid compartments we believed that the patient had been given an excess of water as 5 per cent dextrose solution. This was confirmed about 10 days later by her doctors, as well as by her clinical course.

The hemoconcentration on admission (hemoglobin 16 Gm. per 100 ml. blood decreased by dilution to 10 Gm. on +11 day) was improved by dextran solution and by delivery. The serum proteins despite the hemoconcentration were only 4.4 on admission and decreased to 3.2 Gm. per cent on the third day, but her weight was decreasing and urine increasing, thus indicating again that the edema was due to other factors than the low serum albumin. These serum protein changes suggest loss of protein into the interstitial fluid during the edema-forming stage and return to circulation when edematous fluid is eliminated. It is hard to conceive of regeneration of serum proteins and hemoglobin with a negative nitrogen balance.

Fig. 4 shows the sodium, potassium, chloride, nitrogen, phosphorus and water intake and output in Case 6. There was no electrolyte intake for 5 days and then less than 12 meq. of sodium or chloride per day. The urine

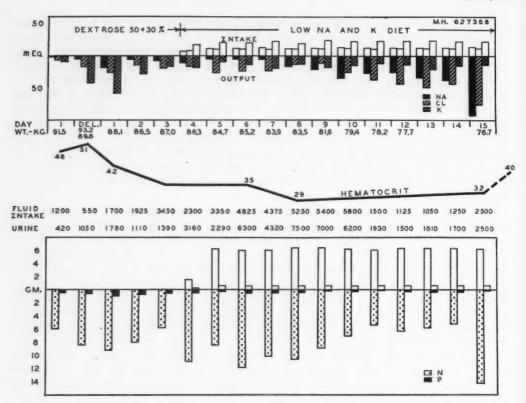


Fig. 4.—Case 6. Shows intake and output. Note the small excretion of sodium and chloride with intake of only dextrose solution and continuance of small excretions until last hospital day. The nitrogen balance was negative on almost every day, but protein intake seemed to increase the loss.

content of these ions was never very large, but in a period of 16 days the patient had adjusted her extra- and intracellular fluid compartments and electrolyte content to such a degree that she was clinically normal except for the proteinuria. She was in a room at constant temperature and humidity while in the hospital. All weights in our hospital were on a sensitive beam balance. The nitrogen loss was considerable as noted by us in all of these edematous patients and we are trying to determine if it is real (loss of body protein) or if it is due to the excretion of retained nonprotein constituents (urea, uric acid, etc.) in the edematous fluid.

Fig. 5 depicts extra- and intracellular changes in water, sodium, and potassium as well as the beam weights. Note the consistent losses of extracellular sodium and increases in the intracellular sodium and decreases of water from both compartments. These changes may be greater or less, since they are based on certain assumptions, but we believe the direction of change is correct.

Comment

All patients with either form of toxemia had been under treatment in the hospital for 24 hours or more, average 4 days, before the tissues were obtained. Thus any differences which were found were presumably greater at the height of the disease. Furthermore, all of our analyses are based on tissue obtained from the rectus muscle where subcutaneous edema is less prom-

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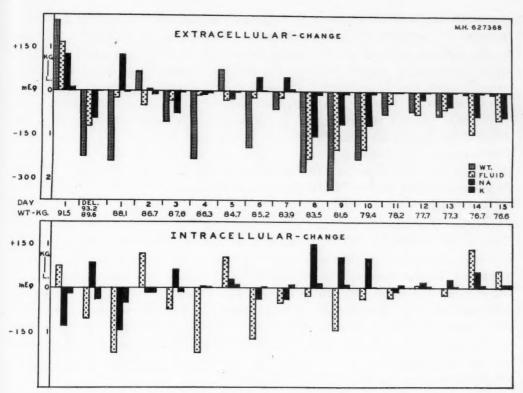


Fig. 5.—Case 6. Shows changes in fluid compartments. Note marked changes in extracellular fluid and electrolytes which are customary and marked changes in intracellular with increase in sodium. A considerable portion of the water came from this space.

inent than in the legs. Muscle edema and electrolyte disturbance are presumably general. Thus, in the few cases where simultaneous biopsies from abdomen and leg and in the four where only tissues from the leg were obtained, there is no significant difference between rectus and gastrocnemius muscle and the two skin samples.

We have over 3,000 determinations of serum electrolytes in normal pregnant, over 1,000 in toxemic patients, including studies from all patients in this report. Blood samples are obtained in a dried syringe without stasis, and the serum is separated from the cells within less than one hour. Longer exposure of serum to cells results in measurable differences in water and electrolytes. We find that for the patients with pre-eclampsia or hypertensive disease the mean values for sodium, chloride, and potassium are essentially the same as those for normal pregnancy. The range for sodium was 127 to 142 meq. and for potassium 3.9 to 5.6 meq., while in the normal term pregnancy the range was 132 to 137 and 4.6 to 5.4 meq. of potassium. There were 2 low values for serum sodium and chloride sodium of 114 and 117 and chloride of 81 and 90 meq., which were due to vomiting or improper treatment.

Our findings were disconcerting. We had expected to find an increased water content in the rectus muscle of pre-eclamptic patients. We also ex-

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pected to find a slight increase of sodium in normal pregnancy and a marked increase in patients with pre-eclampsia. There was a significant increase in the sodium content of the rectus muscle from that of normal pregnant patients but, much to our surprise, the sodium concentration in patients with pre-eclampsia and hypertensive disease was significantly decreased; the values were essentially those of a nonpregnant individual. The fact that both types of toxemia showed values similar to those found in nonpregnant patients indicates an important disturbance of extra- and intracellular electrolytes. Furthermore, the identical values exclude any mistakes in diagnosis between pre-eclampsia and hypertensive disease as being the cause. We have studies in progress which we hope will explain these changes.

We know that in normal subjects there is a balancing mechanism between the plasma, interstitial and intracellular water, and electrolytes; that there is an increase in water in the compartments in normal pregnancy with constant electrolyte equilibrium. The increase in the tissue water may be the cause for the decrease of 5 to 10 meq. of total cations and anions observed in the serum of normal pregnant women. The subcutaneous tissues and other extracellular areas can contain a large amount of excess water and electrolyte before serious signs and symptoms manifest themselves. We are primarily concerned with the water and electrolyte changes, using as indicators sodium and potassium in the rectus muscle as representative of intracellular changes in the various organs of the body.

The similar findings of an increase in the sodium concentration in the skin of normal pregnant patients, but a decrease to nonpregnancy values in the skin from pre-eclamptic and hypertensive patients confirm our findings on the rectus muscle, but again are unexplainable at this time.

Summary

In the normal pregnant patient when compared with the nonpregnant, the following significant changes are noted:

Muscle: The water content is unchanged. Sodium is increased. Potassium remains unchanged. The Na:K ratio is increased. The nitrogen content is unchanged.

Skin: Sodium and water are increased. Potassium is unchanged. The Na:K ratio is unchanged. Nitrogen is slightly lower in wet tissue.

In the patient with pre-eclampsia or hypertensive disease when compared with normal pregnancy the following significant changes are noted:

Muscle: Water is unchanged. Sodium is decreased in pre-eclampsia and hypertensive disease (similar to nonpregnancy values). Potassium is unchanged. The Na:K ratio is less in pre-eclampsia than in hypertensive disease. Nitrogen content is unchanged.

Skin: Water is unchanged. Sodium is decreased in pre-eclampsia and hypertensive disease (similar to nonpregnancy values). Potassium is unchanged. The Na:K ratio is unchanged. Nitrogen in wet tissue is higher from the hypertensive patient than from the normal pregnant or pre-eclamptic patient.

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These results on the sodium content of rectus muscle in pre-eclampsiaeclampsia and hypertensive disease were at variance with published reports and were surprising to us since a hypernatremic muscle offered more opportunity for theorizing. Three separate groups of analysis confirmed this finding. The explanation awaits further studies.

The clinical application was illustrated by three eclamptic patients, each of whom was made markedly worse by the wrong solution and the injudicious administration of excessive fluids.

Our studies indicate that in pre-eclampsia and hypertensive disease there is a significant decrease in the sodium ion concentration of voluntary muscle with a resultant alteration in the sodium-potassium ratio when compared with those of tissues obtained from normal pregnant patients. The fact that the values are essentially those of the nonpregnant woman does not detract from their abnormality.

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Discussion

DR. DUNCAN E. REID, Boston, Mass.—Pregnancy offers a unique opportunity for the investigation of normal and abnormal fluid and electrolyte metabolism. While readily available for study, much remains to be known regarding the fluid and electrolyte retention of pregnancy. In a discussion of the subject it is best to summarize briefly those facts which have attained a certain degree of validity.

Within the limits of accuracy of current methods the plasma volume in normal pregnancy has been found to expand by 25 to 50 per cent while the interstitial fluid is conservatively estimated to increase by 20 to 25 per cent. Disregarding the cause, the concentration of extracellular sodium as reflected by the level of serum sodium is decreased in normal pregnancy. The total sodium content of the body, however, is reputed to be in excess of that required to maintain the isotonicity of the expanded extracellular fluid volume. Consequently, it has been suggested that some of the sodium is retained either in an osmotically inactive form, possibly in bone, or becomes increased within the body cells. Recent studies, however, by Gray and Plentl,1 utilizing radioactive isotopes, have established the magnitude of sodium retention in the last half of pregnancy, which approximates 500 meq. If confirmed, this amount of sodium is not in excess of the amount required for the growth occurring during this period.

In toxemia of pregnancy fluid and electrolyte retention is considered to be accelerated. Plasma volume apparently is not increased to the same extent as in normal pregnancy. In fact, Freis and Kenny² have shown that in patients with severe toxemia the mean plasma volume may not be increased over that in the normal nonpregnant woman. Whatever increase occurs in the extracellular or "available fluid" is confined mainly to the interstitial or extravascular compartment. Indeed, the difference in extracellular fluid in normal or toxemic pregnancy is not necessarily one of volume but of distribution of fluid between the vascular and interstitial compartments. Lambiotte-Escoffier and associates,³ in attempting to measure extracellular fluid and total body water by inulin and antipyrine, respectively, suggest, however, that a portion of the fluid retained in toxemia of pregnancy is intracellular. Again, we are hampered by lack of accurate or precise methods and more studies are indicated.

In our experience the serum concentration of sodium in pregnancy toxemia is appreciably lower than that of normal pregnancy. Whether the amount of sodium retained is in excess of the quantity necessary to maintain the isotonicity of the expanded body fluids remains to be determined. It is this aspect of the problem which has interested Dr. Dieckmann.

Careful studies in nonpregnant patients with a variety of medical conditions have revealed many valuable data concerning the status of the intracellular phase of water and electrolyte metabolism. Experimental alterations in the extracellular environment and in patients with disturbed acid-base balance^{4, 5} have shown significant changes in the water and electrolyte content of the intracellular phase.

Dr. Dieckmann has presented data which we believe, with additional observations, could be expanded to delineate the distribution of fluid and electrolytes in both normal and toxemic pregnancy. We would be interested in the data on the chloride space in the few cases to which the author refers. This information would allow for the eventual calculation of the absolute amounts of intracellular sodium or potassium.⁴

The term tissue water requires a precise definition. Drying tissue to a constant weight does not constitute a measure of intracellular water, since all tissues have an extracellular phase. Dry weight of serum as a representative of extracellular fluid would furnish the necessary information to differentiate between the amounts of intracellular and extracellular water. The sodium content of tissue in the study, therefore, is that contained both in the intra- and extracellular phases. It follows then that the sodium content of tissue can be appraised only when we are in possession of essential data concerning its distribution between the intracellular and extracellular phases of the tissue.

Contrary to previous observations, this paper reveals that the sodium content of the rectus muscle from patients with pre-eclampsia and hypertensive disease was decreased when compared with specimens from normal pregnancy and, in fact, approached the values found in nonpregnant women. The water content of rectus muscle from all patients, pregnant and nonpregnant, did not differ appreciably. Studies of the deuterium space in normal pregnancy indicate that the increase in total body water is commensurate with the increase in total body solids.⁶, ⁷

The interpretation of the differences in sodium and water content which Dr. Dieckmann has presented is difficult for the findings appear somewhat paradoxical. We would offer a suggestion, however, to explain the increased sodium content of muscle in normal pregnancy which does not pertain to muscle from toxemic patients. In toxemic patients the predominant increase in extracellular fluid volume is confined to the interstitial compartment. This, accompanied by a lowered extracellular sodium concentration, would result in a decreased sodium content per unit of tissue mass. By contrast, in the normal pregnant patient there is a more equitable distribution of extracellular fluid between the plasma and interstitial compartments in the presence of a higher serum sodium concentration. Thus, the sodium content of rectus muscle mass accordingly should be higher in normal pregnancy than in pregnancy toxemia.

Finally, caution is necessary when we speak of changes in the isotonic composition or pattern of the cell in normal and toxemic pregnancy, for we imply that the cell is either existing in an abnormal acid-base environment or there is some mechanism peculiar to pregnancy which alters cell membrane permeability.

It is therefore reassuring to learn that the sodium content of voluntary muscle is not significantly altered in toxemia of pregnancy. If the direction of fluid distribution could be controlled, then the edema of pregnancy toxemia might be medically reverted to normal. On the basis of current evidence, I believe this involves the extracellular rather than the intracellular phase.

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- DR. J. ROBERT WILLSON, Philadelphia, Pa.—Dr. Dieckmann's observations are interesting and at the moment perplexing, but they will eventually be explained satisfactorily.

Dr. Dieckmann has reported on the sodium concentration in small amounts of tissue and not on the total body content, but in a condition characterized by decreased sodium excretion, fluid retention, and edema, with normal electrolyte levels in both blood serum and edema fluid, it is difficult to believe that the total electrolyte content would be low or even normal. The sodium concentrations in plasma, interstitial fluid, and cells should equilibrate at a reasonably normal level no matter what the total amount is if cellular function is normal and unless renal function is drastically altered. Therefore no conclusions can be drawn unless the total amount is known.

In Case 6, for instance, if only the electrolyte concentrations are considered it might be difficult to determine what had happened. In this patient the lowest levels of serum, skin, and muscle sodium were found, yet with a maximum total intake of only 120 meq. of sodium the serum levels returned to normal during the first 2 weeks after delivery. Because this patient had been given a large amount of fluid and was oliguric it seems likely that the abnormal electrolyte levels were due to excessive dilution because of a high-fluid, low-sodium intake and inability of the kidney regulating mechanism to function properly. During the puerperium she excreted the excess water as low-sodium urine and the blood and tissue levels returned to normal.

The findings in Case 6 may actually be an exaggerated example of the changes which occur in the whole group of toxemias, but because of the marked alterations in physiologic functions and the excessive administration of water the chemical changes may have been more pronounced than those in the patients with milder disease. Dr. Dieckmann has demonstrated that sodium excretion is impaired even in patients with mild pre-eclampsia; this of course means that water excretion also is delayed and that the extracellular fluid content is higher than in normal pregnancy. The low tissue levels of sodium observed by Dr. Dieckmann in toxemic patients could therefore be in part the result of an attempt to maintain electrolyte equilibrium between the muscle and the edematous extracellular spaces.

Another factor may be present, however. Even though the patients were not actively treated during the observation period the amounts of electrolytes in the tissues undoubtedly changed considerably between the time of admission to the hospital and the time the tests were made. In our own studies we have found that most patients with mild pre-eclampsia will lose several pounds and that edema may disappear during the first 24 hours after they enter the hospital even though they remain ambulatory and on a normal sodium intake. I doubt therefore that the findings on these patients, in whom the specimens were taken after an average of 4 days' hospitalization, represent the true state of the tissues in patients with active pre-eclampsia.

I wonder if the rectus muscle is a suitable one to study. Does the fact that the water contents in the recti were similar in all 4 groups of women mean that muscle water is not increased during pregnancy or only that pressure from the large near-term uterus squeezes some of it out? Before Dr. Dieckmann can be certain of this he should measure the water content of the recti at various stages of pregnancy in both multiparas and primigravidas and in nontoxemic patients with polyhydramnios and multiple pregnancy.

There was little difference in the findings in patients with pre-eclampsia and those with hypertensive disease. Did the latter have only essential hypertension or was there in addition an acute process superimposed? If there were an acute process do the findings suggest to Dr. Dieckmann that the patients might have had pre-eclampsia in addition to essential hypertension?

DR. RUSSELL DE ALVAREZ, Seattle, Wash.—During the past year we have concerned ourselves with the diffusion of water and water vapor through the skin. While we know that the stratum corneum and the stratum basalis are areas in the skin where water may be stored, we have some evidence to show that the diffusion of water actually occurs in the stratum granulosum. Even though sweating, with its high water losses, results from active secretion of the sweat glands, insensible losses of water occur as a result of diffusion of water from the dermis through the epidermis to the surrounding environment. These, of course, would be modified by the surrounding humidity and the temperature of that environment.

Attempting to study these phenomena, we have been measuring the inner osmotic activity of the skin to determine the neutral point, utilizing various solutions of electrolytes, such as magnesium chloride, sodium chloride, and potassium chloride, to determine the rates and direction of diffusion. When the salt solution covers the skin, the neutral point is the relative humidity at the surface of that salt solution where there is no water transferred, and is indicated in percentage.

While the complete report of this work will be the subject of future publication, it is significant that the normal, nonsweating, pregnant patient shows consistent values of around 85 per cent. These are significantly lowered in patients with normal pregnancy during the last two months of pregnancy, that is, when the same patient is followed throughout her pregnancy and serial determinations done. The values are also decreased in pre-eclampsia and in all individuals with edema of any sort, whether or not it be associated with a toxemia. In view of the values of neutral point which we have obtained in the pre-eclamptic patient, approximately 55 per cent, as compared to 85 per cent in the normal individuals, we feel that these values obtained are significant changes in neutral points. Whether a transfer of electrolyte occurs with this transfer of water vapor has not been studied by us, but perhaps Dr. Dieckmann has information in this regard.

DR. DIECKMANN (Closing).—A normal individual has no difficulty in disposing of large amounts of food, water, or electrolytes whether given orally or intravenously. If taken by mouth, he may feel stuffy but within one hour the water and electrolytes have been distributed throughout the body until they can be eliminated. Distribution is into the vascular system, then the interstitial and finally the intracellular spaces. As long as electrolytes and water can diffuse between these three compartments and renal function is normal there is no difficulty.

In severe pre-eclampsia and eclampsia water and electrolytes can diffuse from the vascular system into the interstitial and intracellular compartments, but for some unknown reason diffusion is delayed or does not occur from the interstitial into the vascular bed until some twenty-four to forty-eight hours after the expulsion of the placenta. If one can re-establish this normal path of diffusion, the patient improves clinically.

We have considered most of the questions raised by Dr. Reid and they do not solve the problem.

Dr. Willson has proposed some questions. The total body sodium is increased and his idea of pressure on the rectus muscle is untenable with our findings in the gastroc-

nemius muscle as well as the general concepts of physiology. It is possible that the hypertensive patients did have a superimposed pre-eclampsia; if so, it is not the same disease as occurs in the young primipara with pre-eclampsia.

Sodium diffuses readily but it is not rapidly removed from the body. Two months after sodium²² was injected into my circulation, measurable amounts were still present in my serum. A recent report indicates that in sodium loss in rats, 52 per cent comes from the extracellular, 20 per cent from the intracellular compartment, and 28 per cent from bone.

I wish again to emphasize that in the treatment of toxemic patients, and this is also true for gynecologic patients after operation, be cautious in the amount and type of fluids that you give to them. Do not be misled by high or low serum sodium, chloride, potassium, or other values. Consider the body as a whole.

CESAREAN SECTION IN CINCINNATI, OHIO*

1950 Through 1954

RICHARD D. BRYANT, M.D., CINCINNATI, OHIO

VALUABLE lessons can often be learned from past performances, and it is hoped that this will be true in connection with this study.

Material and Method

Cincinnati is a city with a population of just over five hundred thousand. Its hospitals service an additional 250,000 people in surrounding communities. Eleven hospitals have obstetrical departments. In only eight of the eleven are cesarean sections done; when patients in the other three hospitals are to have a cesarean, they are transferred to one of the eight. Rarely, patients are transferred to Cincinnati hospitals for section from communities up to 50 miles away. In the Cincinnati area over 99 per cent of all deliveries are in hospitals.

Many obstetricians are on the staffs of two, three, and even four of the hospitals, so there is abundant opportunity for free exchange of ideas and the development of comparable standards of professional care. The Cincinnati Obstetrical Society also serves as a focus about which the obstetricians form a close-knit group.

Through the splendid cooperation of the hospital administrators and the record rooms personnel, the author was enabled personally to study the chart of every patient classed as having had a cesarean section, ruptured uterus, or hysterotomy. Approximately 40 specific items of information were tabulated for each patient, and the analysis of these findings constitutes this paper. The five-year period, 1950 through 1954, was chosen because it is the most recent; because local conditions (availability of blood, numbers of trained obstetricians, antibiotics, etc.) were relatively constant for that length of time; and because in a shorter period too few sections are done here to be of much significance.

Incidence

Just over 100,000 deliveries occurred in the Cincinnati area during the period under discussion. It is estimated that roughly half of the deliveries were managed by general practitioners. Just over 2,500 of the deliveries were classed as cesarean sections by the various hospital record departments. On study of the charts, however, it was discovered that nearly all abdominal deliveries were being classed as sections, although several were actually cases of ruptured uterus, far-advanced ectopic pregnancy, or removal of an intact uterus containing a fetus weighing more than 500 grams. Of the total it was decided that only 2,486 fulfilled the requirements of the following definition: cesarean section is the operation in which one or more babies weighing 500 grams or more are removed from an unruptured uterus through incisions in the abdominal and uterine walls.

^{*}Presented at the Sixty-sixth Annual Meeting of the American Association of Obstetricians and Gynecologists, Hot Springs, Va., Sept. 8 to 10, 1955.

The incidence of cesarean section in this study was 2.43 per cent of the total deliveries. The incidence of section in the hospitals where they are performed is slightly higher—2.57 per cent—than in the area as a whole, since the statistics of these eight hospitals include the patients transferred to these hospitals specifically for section. There has been only slight increase in the incidence of section over the five-year period, as shown in Table I.

TABLE I. INCIDENCE OF SECTIONS BY YEARS

*	YEAR	PER CENT SECTIONS
	1950	2.57
	1951	2.47
	1951 1952	2.47
	1953 1954	2.64
	1954	2.69

There was considerable difference in the incidence of sections in the various hospitals. For the five-year period the highest incidence in any one hospital was 3.8 per cent, the lowest 0.9 per cent. The highest incidence in any one hospital in any one year was 4.4 per cent, the lowest 0.5 per cent.

Analysis of Cases

Operators.—

The operations were performed by 65 different private physicians plus an undetermined number of residents. All the recognized obstetricians in Cincinnati perform their own sections. Thirty-four operators performed 10 or fewer sections each. Table II shows the professional status of all the operators, and the number of sections performed by each class.

Table II. Professional Status of Operators and Number of Operations Performed by Each Class

CLASS OF OPERATOR	NO. OF SECTIONS	PER CENT OF TOTAL
Obstetricians	2,057	82.8 1 05 0
Residents	325	13.1 95.9
Surgeons	71	2.9
General practitioners	33	1.3
Total	2,486	

Preoperative Diagnoses and Indications for Section.—

There were almost innumerable preoperative indications for sections. Classification was difficult. The following nine major classifications were evolved.

1. Mechanical obstruction to delivery: all cases of disproportion, malpresentation, and malposition, that is, all cases in which the bony pelvis was thought to be too small to permit the delivery of a baby vaginally, alive and undamaged, plus those cases in which the birth canal was blocked by a tumor.

2. Bleeding: chiefly placenta previa and premature separation of the placenta. Includes a few cases in which vaginal (uterine) bleeding was present, but no specific diagnosis was made preoperatively.

3. Hypertensive disease: toxemia of pregnancy (pre-eclampsia and eclampsia), and chronic hypertension.

4. Fetal indications: fetal distress, prolapsed cord, and suspected Rh incompatibility.

5. Functional anomalies: failure to go into labor, and all sorts of uterine dyskinesia.

6. Abnormalities of the reproductive organs.

TABLE III. PREOPERATIVE DIAGNOSES (INDICATIONS) FOR CESAREAN SECTION

1.	Mechanical obstruction			577
	A. Maternal		451	
	Fetopelvic disproportion	429		
	Obstructing tumor	17		
	Fractured pelvis (healed)	2		
	Asymmetrical pelvis	1		
	Congenital dislocation of hips	1		
	Hip operation (healed)	1		
	B. Fetal		126	
	Transverse lie	63		*
	Breech presentation	23		
	Brow presentation	17		
	Face presentation	11		
	Oblique lie	7		
	Compound presentation	3		
	Parietal presentation	2		
9	Bleeding	-		382
	Placenta previa	234		002
	Premature separation of placenta	143		
	"Bleeding"	3		
	Low-lying placenta	2		
2	Hypertensive diseases	2		95
u.	Toxemia	72		30
		10		
	Essential hypertension (with or without toxemia)			
	Eclampsia Dicheter and towards	9		
A	Diabetes and toxemia Fetal indications	4		56
T.		10		90
	Prolapsed cord	19		
	Fetal distress	35		
E	Rising anti-Rh titer Functional anomalies	2		222
J.		101		222
	Uterine inertia	161		
	Cervical dystocia	24		
-	Prolonged labor	8		
	Membranes ruptured, no labor	8		
	No progress	6		
	Dystrophia-dystocia syndrome	6		
	Postmaturity	3		
	Uterine tetany	2		
	Threatened rupture of uterus	1		
	Failed induction	1		
	Soft-tissue dystocia	1		
_	Dystocia	1		
6.	Abnormalities of the pelvic organs			53
	A. Congenital		9	
	Double uterus	5		
	Hypoplastic vagina	3		
	Uterine diverticulum	1		
	B. Acquired		44	
	Cervical stenosis	12		
	Vaginal repair	10		
	Fibroids	8		
	Uterine scars, various	7		
	Vulvar varices	4		
	Vaginal infection and edema	1		
	"Fibrotic uterus"	1		
	"Previous uterine surgery"	1		
7	Concurrent and intercurrent diseases			42
	Diabetes	23		
	Heart disease	6		
	Mental disease (psychosis)	2		
	Carcinomatosis	ĩ		
	Melanosis	1		
	Carcinoma of breast	1		
	Poliomyelitis (terminal)	i		

TABLE III-CONT'D

Cerebral hemorrhage	1	
Osteogenesis imperfecta	1	
"Acute abdomen"	1	
Aneurysm of circle of Willis	1	
Aortic thrombosis	1	
Hyperemesis	1	
Thrombocytopenic purpura	1	
8. Miscellaneous		45
Elderly nulliparity	17	
Previous obstetrical difficulty	12	
Failed forceps	9	
Extravaluable baby	3	
Pathological fear of labor	2	
Term pregnancy	1	
Patient's request	1	
		1,472
9. Previous section		1,014
Total		2,486

- 7. Concurrent and intercurrent diseases.
- 8. Miscellaneous.
- 9. Previous section.

In many cases there were multiple indications for section. To simplify classification, what appeared to be the most urgent or important indication was chosen. This causes apparent discrepancies when specific diagnoses are discussed later.

Table III shows in detail the preoperative diagnoses and indications for section for the entire series.

The most baffling diagnosis was "term pregnancy." There was no other diagnosis on the chart. One of the most honest diagnoses was "patient's request."

Types of Section .-

Table IV shows the types and numbers of operations performed.

TABLE IV. TYPES OF SECTION EMPLOYED

TYPE OF OPERATION	NUMBER	OF CASES	PER CENT OF TOTAL SECTIONS
Lower segment		2,172	87.3
Transverse incision	1,460		
Longitudinal incision	556		
Type incision unknown	156		
Classical		228	9.0
With hysterectomy		45	1.8
Supravaginal	31		
Total	14		
Miscellaneous		12	
Extraperitoneal	9		
Peritoneal exclusion	1		
Transverse fundal	1		
Vaginal	1		
Type not specified		29	
Total		2,486	

There has been a slight increase in the lower segment operation, from 85 per cent in 1950 to 90 per cent in 1954. The transverse incision is becoming increasingly popular, accounting for 53 per cent of all the lower segment operations in 1950 and 71 per cent in 1954.

The Pfannenstiel incision was used 44 times (1.8 per cent).

The indications for hysterectomy were as given in Table V.

TABLE V. INDICATIONS

PREOPERATIVE DIAGNOSES	NO. OF	CASES	
Fibroids		19	
Hemorrhage following delivery of placenta		14	
Premature separation of the placenta	5		
Placenta previa	1		
"Bleeding"	1		
Previous section	3		
Disproportion	2		
Toxemia	1		
Inertia	1		
Thin scar (of previous section)		8	
Placenta accreta		1	
Intrauterine infection		1	
For sterilization		1	
No reason given		1	
Total		45	

While not, by definition, properly included here, the one vaginal section might be of some interest.

The patient was a multipara for whom labor was induced electively at term by artificial rupture of the membranes and a Pitocin drip, in spite of a double footling presentation. The cord prolapsed when the cervix was 4 cm. dilated. No operating room was available, so the patient was placed on a delivery table in lithotomy position, the anterior vaginal wall was dissected free from the cervix, and the bladder was pushed upward. A 3 inch incision was made in the anterior wall of the cervix and lower uterine segment. A 7 pound, 14 ounce baby in good condition was delivered by breech extraction. The incision did not extend, and was easily repaired. Bleeding was moderate. One transfusion of 500 c.c. of blood was given. The postoperative course was uncomplicated and afebrile.

Anesthetics.

Nearly 7 out of every 8 patients (86 per cent) were operated on under spinal anesthesia. The drug of choice was Pontocaine. All the spinal anesthetics were given as a single dose, except one. In a very few cases the anesthetic, in hypobaric solution, was given with the patient in the knee-chest position (prolapsed cord).

The dosage range of Pontocaine was rather wide, although most of the patients received doses ranging from 5 to 10 mg.

Premedication varied widely. Many patients received none. Atropine, hyoscine, or scopolamine was commonly given intravenously just prior to the injection of the spinal anesthetic. Barbiturates were seldom used.

In 10 per cent of the operations, inhalation anesthesia was used, mostly cyclopropane or nitrous oxide-oxygen-ether. In a few cases, intravenous anesthesia was used. Local anesthesia was the least popular (25 cases). One of these was an intercostal block in a patient with multiple sclerosis.

Table VI is a summary of the anesthetics used.

TABLE VI. TYPE OF ANESTHESIA USED IN CESAREAN SECTIONS

TYPE OF	NO. OF	PER CENT
ANESTHETIC	CASES	OF TOTAL
Spinal	2,140	86.0
Inhalation	257	10.3
Intravenous	53	2.1
Local	25	1.0
Unknown	11	0.6
Total	2.486	

There were no maternal deaths attributed to the anesthetic.

Approximately 88 per cent of the anesthetics were administered by physicians (anesthesiologists), the remainder were administered by nurse anesthetists. Practically all of the latter were in one hospital.

X-rays.

The use of x-ray examination for obstetrical diagnosis is not very common in Cincinnati hospitals. Nevertheless, 28 per cent of all the patients in this series had x-ray examination prior to operation. It was far commoner to have x-rays made prior to primary or first sections (45 per cent) than preceding repeat sections (5 per cent). One-fifth of all bleeding patients had x-rays. Over half (58 per cent) of nonbleeding patients had x-rays prior to primary section.

Sterilization.

Deliberate sterilization of patients is permitted in five of the eight hospitals. Neither specific permission of a staff committee nor recommendation of a consultant was generally required during the period under consideration. The Pomeroy technique was commonly employed. In a few cases the Irving method was used. Only rarely was the Madlener method utilized. Hysterectomy primarily for sterilization may have been done a few times.

Nineteen per cent of the 1,764 patients delivered by section in the five hospitals where sterilization is permitted were sterilized. Table VII shows the section following which sterilization was performed, and the percentage of patients in each classification.

TABLE VII. STERILIZATION IN RELATION TO NUMBER OF SECTIONS

SECTION FOLLOWING WHICH STERILIZATION WAS PERFORMED	TOTAL NO. OF PATIENTS	NO. OF STERILIZATIONS	PER CENT STERILIZED
First	1,048	81	7.7
Second	563	162	28.7
Third	120	73	61.3
Fourth	23	11	47.6
Fifth	4	3	75.0
Unknown	6	1	

The indication for sterilization was usually not stated or was not clear-cut. The vast majority appeared to have been done simply on the basis of some arbitrary rule concerning the danger of repeated sections. Certainly there was no hard-and-fast rule followed. Only a relatively few patients had medical or psychiatric complications which alone seemed to justify the procedure. Multiparity no doubt was the real indication in most of the cases in which sterilization followed the first section in multiparas. There was little or no indication that cesarean section was done primarily for the purpose of sterilization.

TABLE VIII. INDICATIONS FOR SECTIONS IN 14 CASES IN WHICH STERILIZATION FOLLOWED DELIVERY OF THE FIRST VIABLE CHILD

Essential hypertension complicated by pre-eclampsia	4
Diabetes	2
Multiple sclerosis	1
Osteogenesis imperfecta	1
Psychosis	1
Rheumatic heart disease	1
Previous hysterotomy	1
Deaf mute	1
Not indicated	2

In 14 cases sterilization followed the delivery of the first viable child. The indications for the sections (and presumably for the sterilization) are shown in Table VIII.

Five patients in this series had previously been sterilized since 1950 following section in Cincinnati. In other words, of 326 sterilizations during the period under discussion, 5 (1.5 per cent) are known to have failed, and resulted in subsequent pregnancy, cesarean section, and resterilization. This failure rate, 1.5 per cent, may, however, be grossly inaccurate.

Incidental Operations .-

A variety of procedures, other than hysterectomy and tubal ligation, were performed at the time of section. Table IX shows what these other operations were.

TABLE IX. INCIDENTAL OPERATIONS ASSOCIATED WITH CESAREAN SECTION

Myomectomy	29	
Ovarian and parovarian cystectomy	22	
Herniorrhaphy	17	
Appendectomy	16	
Removal of ovarian tumors	2	
Fibroma 1		
Thecoma 1		
Salpingectomy	2	
Bilateral oophorectomy, lipectomy,		
perineorrhaphy, Gilliam suspension,		
bowel resection, hemorrhoidectomy,		
correction of diastasis recti,		
toenail removal, presacral		
neurectomy—each 1	9	

Antibiotics.—

The antibiotics were used freely; 65 per cent of all the patients received them. Their chief use was prophylactic, starting immediately after the operation; 57 per cent of all the patients received antibiotics in this manner.

Transfusions .-

Blood is readily available in all the Cincinnati hospitals, through their own blood banks or through the University of Cincinnati Blood Transfusion Service. No so-called Red Cross blood is ordinarily available here.

It is customary, although not mandatory, to have two units of compatible blood ready and instantly available prior to section. In none of the hospitals is type O, Rh-negative blood regularly reserved for the obstetrical services.

Patients who are bleeding or suspected of bleeding prior to section are, of course, more likely to require transfusion than those who are not bleeding. In this series there were 398 patients bleeding and 2,088 not bleeding. In the group of 398 bleeding patients, 96 per cent had blood ready prior to operation, and 86 per cent actually received blood. For the group of 2,088 who were not bleeding, blood was ready in 84 per cent and was given to 31 per cent. For the entire series, blood was ready in 86 per cent of the cases and was given to 39 per cent.

The use of blood was nearly uniform over the entire period.

Morbidity.

For various reasons, the figures for maternal morbidity in this series are grossly inaccurate, so they will not be presented.

An interesting, and possibly significant, fact was revealed by the morbidity studies in purely elective sections, although it must be emphasized that the figures may not be a reflection of the true incidence of morbidity. Nevertheless, with factors of error entering equally into two groups nearly equal in size, perhaps they reflect the true situation with a certain degree of accuracy.

Of 873 patients operated on electively, slightly less than half (401) received antibiotics prophylactically, and slightly more than half (472) did not receive them prophylactically. On the basis of these figures, 7.1 per cent of the first (prophylactic) and 8.3 per cent of the second (nonprophylactic) group had temperature elevations which would be classified as morbid by the standards of the American Committee on Maternal Welfare. The difference is so slight as to suggest that in elective cases the use of antibiotics prophylactically is of little value in preventing morbidity.

Primary and Secondary Sections .-

Fifty-nine per cent of the sections in this series were primary or first sections, 41 per cent were repeat sections. Table X shows which sections the patients in this series underwent.

TABLE X. FREQUENCY OF PRIMARY AND SUBSEQUENT SECTIONS

SECTION NUMBER	NO. OF PATIENTS
1	1,467
2	764
3	198
4	42
5	7
6	2
Unknown	6
Total	2,486

While the total number of sections done was 2,486, only 2,041 separate patients were involved. Table XI shows how many sections individual patients underwent in the five-year period.

TABLE XI. FREQUENCY OF MULTIPLE SECTIONS IN THE SAME PATIENT

	NO. OF PATIENTS	TOTAL NO. OF SECTIONS
1 section	1,646	1,646
2 sections	349	$\substack{\textbf{1,646}\\698}$
3 sections	42	126
4 sections	4	16
Total	2,041	2,486

One of the most remarkable patients had a section on the same date three years in a row, then had a fourth section 18 months later.

The preoperative diagnoses in primary sections were essentially those in Classes 1 through 8, as shown in Table III. Table XII gives a brief summary of the major indications for primary section.

TABLE XII. MAJOR INDICATIONS FOR PRIMARY SECTION

PREOPERATIVE DIAGNOSIS	NO. OF PATIENTS	PER CENT OF PRIMARY SECTIONS
1. Mechanical obstruction	576	39.0
2. Bleeding	379	26.0
3. Hypertensive diseases	95	6.5
4. Fetal indications	55	3.8
5. Functional anomalies	222	15.0
6. Abnormalities of the pelvic organs	53	3.6
7. Concurrent and intercurrent diseases	42	2.9
8. Miscellaneous	45	3.2
	1,467	

Mechanical obstruction, bleeding, and functional anomalies accounted for 80 per cent of the indications for primary section.

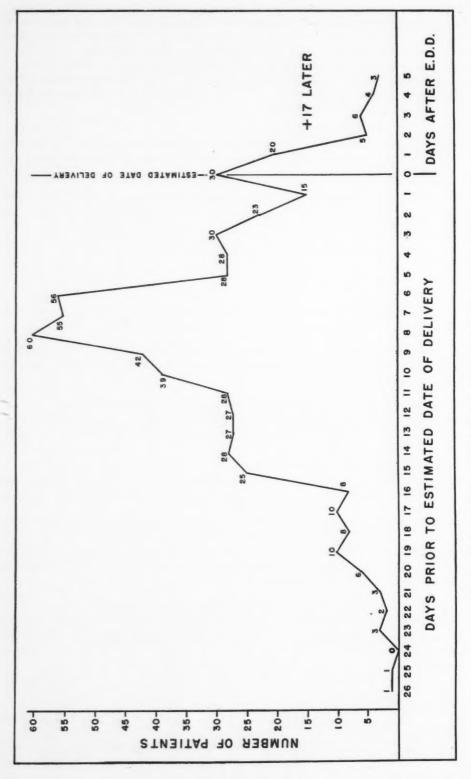


Fig. 1.—Date of elective repeat section, 648 of 719 cases. Dates unknown in 71.

There were 1,019 patients who had previously been delivered by section. The succeeding sections were done under the circumstances shown in Table XIII.

TABLE XIII. CIRCUMSTANCES UNDER WHICH REPEAT SECTIONS WERE PERFORMED

PREOPERATIVE DIAGNOSES AND INDICATIONS FOR REPEAT SECTION		NO. OF PATIENTS	PER CENT OF RE
Elective repeat section		719	70.7
Ruptured membranes, no labor		35	3.4
Admitted for elective section, labor after		17	1.7
admission			> 19.2
Labor		178	17.5
With intact membranes	150		
With ruptured membranes	27		
With diabetes	1		
Bleeding		23	2.3
Premature separation of placenta	10		
Placenta previa	7		
Unspecified	6		
Essential hypertension and/or toxemia		19	
Rising anti-Rh titer		9	
Abdominal pain		8	
Diabetes		6	
Rheumatic heart disease		2	
Eclampsia		1	
Pyelitis		î	
Intestinal obstruction		1	

Four of the patients who had repeat section died (see Maternal Mortality Cases 7, 8, 10, and 11). There were 11 stillbirths in this group. Five newborn infants died—a gross neonatal mortality rate of 0.7 per cent. Two of these babies had congenital anomalies incompatible with life. The corrected neonatal mortality rate is therefore 0.4 per cent.

About 70 per cent of the patients who had previously had sections were

operated on electively.

While there are no statistics on this point, it is my impression that very few patients in Cincinnati are delivered vaginally after once having had a section—probably fewer than 5 per cent. In this series of patients, 7 are known to have had vaginal deliveries between sections.

The date selected for purely elective repeat section was usually within two weeks of the estimated date of delivery. The favorite time was 6 to 10 days before term (Fig. 1).

Elective Sections .-

Cesarean section was performed electively in 873 cases. The term "elective" is used here to indicate the absence of obstetrical, medical, or other complication which would probably have influenced the immediate outcome for either the mother or baby. The patients were not in labor, and the membranes were intact. The indications for the operations are given in Table XIV.

As can be seen, the vast majority of the elective sections were done because of a previous section. Purely elective sections represented 35 per cent of all the sections.

Three sets of twins were encountered among the 873 elective sections, so 876 babies were born. Of these babies, 47 (5.4 per cent) were premature by weight (weighed less than 2,500 grams or 5 pounds, 8½ ounces), in spite of the fact that the delivery date was chosen arbitrarily. Seven of the babies died neonatally, a mortality rate of 0.8 per cent. (There were, of course, no stillborn infants in this group.) Three of the babies who died had con-

genital defects incompatible with life (hydrocephalus, spina bifida, congenital heart defect). The corrected fetal mortality rate is thus 0.47 per cent. Two of the babies who died neonatally were of term size, 2 were premature.

TABLE XIV. INDICATIONS FOR ELECTIVE SECTIONS

INDICATION FOR ELECTIVE SECTION	NO. OF PATIENTS
Previous section	719
Disproportion	65
Transverse lie	13
Breech	10
Elderly nullipara	10
Uterine scar, other than section	9
Obstructing tumor	7
Uterine fibroids	6
Previous obstetrical difficulty	6
Vaginal stenosis or repair	5
Oblique lie	5 3 3
Cervical stenosis	3
Varicose veins	3
Previous stillbirth, double uterus, face presentation, previous hip operation, healed pelvic fracture—each 2	10
Osteogenesis imperfecta, carcinoma of the breast, hematuria, "malpresentation"—each 1	4
Total	873

Placenta Previa .-

The total number of patients who actually had placenta previa was 249. The classical signs of premature separation of the placenta—abdominal pain and tenderness and uterine tetany, and, at operation, visible infiltration of the myometrium, and bloody fluid in the abdominal cavity—were present 6 times although the location of the placenta was that of placenta previa. This combination of complications is seldom described in the literature, and by commonly accepted definition is impossible, since premature separation of the placenta is defined as separation of the normally implanted placenta.

Eighty-three per cent of the patients were nulliparas, 17 per cent multiparas,

Vaginal examination was made prior to operation in 131 cases (52 per cent). The double setup procedure was carried out 48 times (36 per cent).

X-rays were not commonly resorted to as an aid in diagnosing the position of the placenta when placenta previa was suspected. X-rays were used in 53 cases (21 per cent of the total). The results were equivocal, to say the least, and help explain why x-rays are so seldom used for this purpose in this area.

The sections for placenta previa were done as emergencies or semiemergencies (within 24 hours of admission) in 75 per cent of the cases. In the remaining 25 per cent the operation was delayed from 1 to 64 days. In the 61 cases in which immediate operation was not done, the periods of delay were as shown in Table XV.

TABLE XV. DELAY PERIODS FROM ADMISSION, BLEEDING, TO OPERATION FOR PLACENTA PREVIA

DELAY PERIOD	NO. OF CASES
 1 to 5 days	32
6 to 10 days	18
11 to 15 days	3
16 to 20 days	4
36 to 40 days	1
More than 40 days	3
Total	61

One mother died, a maternal mortality rate of 0.4 per cent.

Five sets of twins were among these cases, so the total number of babies involved was 254. Of these, 40 failed to survive, a gross fetal loss of 15.7 per cent. Fetal loss is detailed in Table XVI.

TABLE XVI. FETAL LOSS IN PLACENTA PREVIA

Total term babies		152
Total term babies lost		11 (7.2%)
Stillbirth	6	, , , , , , , , , , , , , , , , , , , ,
Neonatal death	5	(3.4% of term liveborn infants)
Total premature babies		102
Total premature babies lost		29 (28%)
Stillborn	4	(-,0,
Neonatal death	25	(25% of premature liveborn infants)

Neonatal deaths of premature infants were in direct relation to the degree of prematurity.

Neonatal death rates among premature infants delivered by sections from mothers with placenta previa were compared with neonatal death rates among all premature babies delivered by section (except where direct threat to the baby—prolapsed cord, Rh incompatibility, bleeding, and fetal distress—was present). These figures are given in Table XVII.

TABLE XVII. NEONATAL DEATH RATE (PREMATURITY AND PLACENTA PREVIA) COMPARED TO OTHER NEONATAL DEATH RATES

BIRTH WEIGHT	NEONATAL DEATH RATE, PLACENTA PREVIA	NEONATAL DEATH RATE OF BABIES NOT DIRECTLY THREATENED
500-1,000 grams	100%	100%
1,001-1,500 grams	58%	47%
1,501-2,000 grams	33%	10%
2,001-2,500 grams	12%	11%

It is immediately apparent that the neonatal death rate among premature infants weighing between 1,000 and 2,000 grams was higher when placenta previa was present than when it was not. This suggests that the high neonatal death rates among prematures when placenta previa is present may be due not only to prematurity, but also to some lethally depressing effect of the partial interruption of the continuity of the uteroplacental circulation. Almost exactly the same results were found in premature separation of the placenta.

TABLE XVIII. NEONATAL FETAL LOSS RELATED TO DURATION OF PREGNANCY AND TIME OF OPERATION

WEEKS PREGNANT	% FETAL LOS	DIED DURING		
AT ONSET OF BLEEDING	SECTION IN LESS THAN 24 HOURS	SECTION AFTER 24 HOURS	DELAY PERIOD (STILLBORN)	
30	100	50		
31	67	No deaths		
32	42	33		
33	25	No deaths	7 hours—1 baby	
34	19	16		
35	18	No deaths		
36	18	No deaths	15 hours—1 baby	
\			69 hours-1 baby	
37	16	No deaths		
38	No deaths	No deaths		
39	No deaths	No deaths	5 hours—1 baby	
40	No deaths	13		
41	4	No deaths		

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Avoidance of immediate operation is often advocated in placenta previa. The relationship of fetal loss to duration of pregnancy and time of operation is shown in Table XVIII.

While the number of babies in any one category is probably too small to have any real significance, these figures do suggest that up to the end of the thirty-seventh week, the chances for the survival of the baby are improved, in patients with placenta previa, if operation is delayed, but that near term this is not true. The mother must also be considered, however, and many of the immediate operations probably were obviously necessary, irrespective of the fetal outcome. The loss of the 4 babies during the period of delay is, of course, regrettable. It is possible that all 4 could have been saved had operation been done more promptly.

Premature Separation of the Placenta .-

Premature separation of the placenta was present in 139 patients. About 56 per cent were multiparas, 44 per cent nulliparas.

In 12 cases there was no external bleeding.

One mother died, a maternal mortality rate of 0.7 per cent. It may be of

some significance that none of these patients died of fibrinogenopenia.

Fetal loss was extremely high, the highest associated with any of the major complications of pregnancy. Two sets of twins were among the babies delivered, so we are concerned here with 141 babies. Of these, 58 (41 per cent) failed to survive. However, of the 58, 45 were stillborn. Of the 96 liveborn, 13 died neonatally, a mortality rate of 13.5 per cent, almost identical with the neonatal loss in placenta previa.

Prolapsed Cord .-

Prolapsed cord was present and diagnosed 20 times. Four babies failed to survive (20 per cent). Two were stillborn, 2 died neonatally. The fetal survival rate (80 per cent) is far superior to the local fetal survival rate when delivery in similar cases is vaginal.

Maternal Mortality .-

Eleven of the patients in this series are known to have died within less than a year of the operation. Their histories follow:

CASE 1.—This patient, seven months pregnant, was found unconscious at home. She was admitted to the hospital immediately, where a diagnosis of cerebral hemorrhage was made. There was no visible edema, and the urine and blood pressure were normal. Labor started shortly after admission. A classical section was performed to prevent any increase in intracranial pressure due to labor. The patient died 21 hours after operation. Necropsy was not done. Final diagnosis—intracranial hemorrhage, etiology unknown.

CASE 2.—This patient had previously had an intracranial hemorrhage due to the rupture of an aneurysm of the circle of Willis. Elective section was performed near term to prevent increased intracranial pressure due to labor. The patient did well until the sixth post-operative day, when, following a complaint of severe headache, she lapsed into coma. The diagnosis was rupture of a second aneurysm. The patient died on the ninth postoperative day. No necropsy was performed. Final diagnosis—intracranial hemorrhage following rupture of a congenital aneurysm of the circle of Willis.

CASE 3.—This patient had widespread metastases of a malignant melanoma. Her condition became so poor that a section was done to save the baby. The patient lived eleven days after the operation, and died of the melanoma.

CASE 4.—This patient was admitted near term with rapidly progressing poliomyelitis of the bulbar type. Section was done to save the baby. The patient died of poliomyelitis three days postoperatively.

CASE 5.—This patient's pregnancy was terminated at 28 weeks because of essential hypertension complicated by superimposed pre-eclampsia. She recovered from the operation and was discharged from the hospital improved. She returned to the hospital three months later and died of malignant hypertension.

Case 6.—This patient's pregnancy was terminated at 32 weeks because of widespread metastases of breast carcinoma. She died about nine months postoperatively of carcinomatosis.

CASE 7.—Elective repeat section was performed on this patient with essential hypertension. She was discharged from the hospital in good condition. She returned to the hospital, in extremis, nine days after discharge. No necropsy was performed. Probable diagnosis—pulmonary embolus.

CASE 8.—This patient, who previously had had a section, was extremely obese, had massive varicose veins, essential hypertension with superimposed pre-eclampsia, and a gigantic baby. Repeat section was done after labor started. The 12 pound, 8 ounce baby survived. The patient did well for 12 hours, and then suddenly became extremely short of breath and cyanotic and died within half an hour. Necropsy revealed massive pulmonary artery embolism.

CASE 9.—This patient developed severe premature separation of the placenta. Section was performed and the patient was returned to her room. Before arriving there she went into deep shock and died in spite of heroic treatment. Blood for transfusion had not been obtained before operation, and death occurred before blood could be secured.

Case 10.—This patient, who had had a previous cesarean section, went into labor and had a repeat section done promptly. The anesthetic was spinal, with 8 mg. of Pontocaine. Following delivery of the baby, and immediately after the administration, intravenously, of an ergot preparation, the patient collapsed and died within 3 or 4 minutes. Necropsy revealed no cause of death. There was no evidence of pulmonary amniotic fluid embolus. Final diagnosis—acute poisoning due to ergot.

Case 11.—This patient had previously had a section. She was admitted to the hospital when 29 weeks pregnant because of bleeding, presumably due to placenta previa. After eight weeks in the hospital, and now 37 weeks pregnant, the bleeding increased, and a section was done. The anesthetic was spinal, with 3 mg. of Pontocaine. The patient reacted exactly like the one in Case 10, following intravenous ergot. Stimulation and cardiac massage failed, and the patient was pronounced dead. Nearly half an hour after apparent death the patient revived, but was essentially decerebrate. She died five weeks later of pneumonia.

Did cesarean section cause any of these deaths? Is it reasonable to assume that any of these patients would have lived had they been delivered vaginally? It seems probable that the first 6 patients—who died. respectively, of cerebral hemorrhage, rupture of an aneurysm of the circle of Willis, melanosis, poliomyelitis, malignant hypertension, and carcinomatosis—would have died as soon or sooner following vaginal delivery (perhaps 2 or 3 would have died undelivered).

Patients 7 and 8 died of pulmonary embolism. Perhaps No. 7 would not have died had she been delivered vaginally. There are, however, few if any statistics proving that the hazard of death due to embolism following repeat section is greater than the hazard of delivery from below. It is likely that Patient 8 would have required craniotomy had delivery vaginally been attempted.

Probably Patient 9 need not have died. The routine precaution of having blood ready prior to operation on bleeding patients was ignored. The outcome might well have been the same, however, had the same physician delivered the patient vaginally.

Patients 10 and 11 were thought to have died of some peculiar reaction to ergot given intravenously. Abnormal and nearly complete coronary constriction has been postulated. The relationship of cesarean section to this reaction is not known.

As has been pointed out many times, it is important to differentiate between deaths due to cesarean section and deaths following cesarean section. It does not appear that any of these deaths were due to the operation, although this point of view is debatable. Certainly no specific hazard inherent in the operation is evident.

Fetal and Neonatal Mortality .-

There were 2,513 babies delivered in these 2,486 operations, including 25 sets of twins and one set of triplets. Of these babies, 87 were stillborn and 2,426 liveborn. Of the liveborn, 103 (4.2 per cent) died before discharge from the hospital, and 2,323 survived. The total fetal loss was 190 (87 stillbirths and 103 neonatal deaths), a gross fetal loss of 7.6 per cent.

The stillbirths were associated with the complications detailed in Table XIX.

TABLE XIX. STILLBIRTHS AND COMPLICATIONS OF PREGNANCY

Bleeding	57
Premature separation of the placenta 46	
Placenta previa	
Transverse lie	5
Prolonged labor	4
Diabetes	3
Prolapsed cord, Rh sensitization, failed forceps, pre-	
eclampsia, each 2	8
Intrauterine infection, congenital anomalies, compound presentation,	
eclampsia, obstructed labor (fibroid), each 1	5
No cause	5
Total	87

It seems unlikely that any of these babies would have survived had vaginal delivery been elected.

There were 103 liveborn babies who died before leaving the hospital. Slightly over 70 per cent were premature. Of 338 liveborn premature infants, 70 (21 per cent) died. Of 2,002 term liveborn infants 33 (1.6 per cent) died. Forty-two (41 per cent) of all the neonatal deaths were associated with bleeding (placenta previa and premature separation of the placenta), although these complications were present in fewer than 16 per cent of the total cases.

For comparison, figures were obtained from two of the large premature services in the city. During an arbitrarily chosen period of years, these two services took care of 2,752 prematures, of which 2,676 were delivered vaginally. Table XX shows neonatal mortality among prematures delivered vaginally as compared with prematures delivered by cesarean section.

TABLE XX. NEONATAL DEATHS AMONG PREMATURE INFANTS DELIVERED VAGINALLY AND BY SECTION

BIRTH	VAGINAL DELIVERIES		DELIVERY BY SECTION		NEONATAL DEATH RATE	
WEIGHT (GRAMS)	LIVEBORN	NEONATAL DEATH	LIVEBORN	NEONATAL DEATH	VAGINAL (%)	SECTION (%)
500-1,000	160	149	6	6	93	100
1,001-1,500	250	128	33	15	51	45
1,501-2,000	565	94	96	24	17	25
2,001-2,500	1,701	26	201	23	1.5	11.4

It is obvious that liveborn premature infants in the first two weight categories have about the same prognosis whether delivered vaginally or by section. In the two groups of larger prematures, vaginal delivery appears to offer the babies a definitely better chance. This may not be strictly true, however. The babies delivered vaginally are those who lived long enough to get to the premature nursery, and does not include those who gasped a few times in the delivery room, then died. Also removed from the vaginal delivery statistics are those babies delivered alive by section who would have been still-born had they been delivered vaginally.

Comment

As was pointed out in the opening paragraphs, there is a tendency for the record rooms in Cincinnati to classify all abdominal deliveries—whether true cesarean sections, ruptured uterus, far-advanced ectopic pregnancy, or removal of a uterus containing a theoretically viable child—as cesarean sections. Perhaps this is not a very vital point, but medicine in general and obstetrics in particular have always suffered from a lack of precise definitions. A specific example is ruptured uterus. Not one of the current textbooks includes ruptured uterus as an indication for section. Yet, in at least 28 of more than 75 articles on cesarean section which have appeared in the American Journal of Obstetrics and Gynecology since 1945, cases of ruptured uterus were included in the section statistics. Since the prognosis for mother and baby is so different for the two conditions, perhaps we should redefine and re-emphasize the definition of the operation cesarean section.

An obstetrical concept which is difficult to explain to medical students is the fact that, by definition, the mechanism of premature separation of the placenta is inoperative if the placenta is attached wholly or partially to the lower uterine segment. Although it is not universally agreed to, in a general way it might be said that in placenta previa, traumatic separation of the placenta, violent labor, and sudden decompression of the uterus, bleeding follows separation of the placenta, whereas in abruptio placentae (premature separation of the placenta) retroplacental bleeding is the cause of the separation. In view of the fact that six independent operators in this series observed typical separation of the placenta (abruptio) in conjunction with placenta previa, and that current definitions of placenta previa and premature separation, although hallowed by tradition, are inadequate, perhaps an attempt should be made to redefine these complications.

It is often argued that vaginal delivery is safer for the baby than is delivery by section. I believe that if any obstetrician delivered 1,000 consecutive patients vaginally, his fetal results would be worse than if he delivered a similar 1,000 patients by section. The statistics which are usually compared are the fetal results following elective cesarean section and following vaginal delivery. Perhaps there is a fallacy here. It might be more logical to contrast fetal loss following elective section with all fetal loss after the ideal date for elective section, no matter what the type of delivery. In this series, for instance, there were 29 stillbirths and 16 neonatal deaths among babies delivered by

section after the end of the thirty-eighth week of pregnancy. Had these 45 babies been delivered by elective section at the end of the thirty-eighth week of pregnancy, theoretically not more than one of them would have died. It was planned originally that they be delivered vaginally, yet circumstances caused their death and removed them from vaginal delivery statistics. Certainly elective section does not guarantee a living baby, but neither does failure to deliver by elective section, as 45 women in this series can testify. It is my impression that cesarean section could be used sooner and more often in Cincinnati. This statement is based not only on the fact that the incidence of section is low, but also on the testimony of the majority of the obstetricians concerned. They are almost unanimous that they have never performed a section which they were later sorry they had done, but many times have delivered babies vaginally that they afterward wished they had delivered by section. There may also be considerable merit in delivering the extravaluable baby by elective section.

No maternal mortality rate has been presented for this series of cases. Six of the eleven patients who died would certainly have died no matter how delivered. Two others died of embolism. It is to be hoped that this type of complication can be prevented in the future. Two patients died almost instantly following the injection, intravenously, of an ergot preparation. These cases were mentioned here several years ago in a brief discussion of Dr. Gordon's paper on section deaths in Brooklyn. There have been similar deaths reported from other parts of the country. The relationship between the injections and the deaths cannot be established beyond a doubt. No similar deaths have occurred since the abandonment of this type of medication. This proves nothing, since the reaction must be very rare. Nevertheless, we believe that intravenous ergot is contraindicated in cesarean section, especially if the patient is under spinal anesthesia. The death of the patient who had premature separation of the placenta is indefensible. Blood was not ready, nor was blood given until the patient was moribund. Careful attention to details is paramount in cesarean section. In general these statistics support Greenhill's observation that section adds little if any to the chances of maternal death.

The depressing effect of partial interruption of the uteroplacental continuity (as in premature separation of the placenta and placenta previa) is fairly clear-cut in the series, especially among premature babies. The neonatal death rate is appreciably higher than would be expected from prematurity alone. The administration of oxygen to these mothers before delivery might have helped some.

The 80 per cent salvage rate in prolapsed cord suggests that, when feasible, section is the treatment of choice.

No valid conclusions could be drawn concerning Rh incompatibility and section.

The 5 per cent incidence of premature infants delivered by elective section is to be deplored, of course. In many of the cases the prematurity was more evident than real; the baby who at term is going to weigh 2,750 grams (6)

pounds, 1 ounce) may weigh less than 2,500 grams at thirty-eight and a half weeks. In any case, the delivery of premature babies by elective section calls for a study of means of determining the degree of development of undelivered babies rather than the abandonment of elective section.

These statistics are offered with neither pride nor shame, but rather as evidence of how the recommendations of the leaders in our specialty are being translated into everyday obstetrical practice. Improvement is always possible, and now that we know what our local problems are, our results should be better in the future.

The cooperation of the administrators of the Jewish, Bethesda, Christ, Deaconess, Good Samaritan, Cincinnati General, St. Mary, Lady of Mercy, and Children's Hospitals is herewith gratefully acknowledged. I also wish to express to the record room personnel of these hospitals my deep appreciation of their tireless and cheerful labors in making more than 2,600 charts available for study.

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Discussion

DR. SILAS H. STARR, Louisville, Ky.—Studying the analysis of cesarean sections in Cincinnati led me to compare some of the findings with those in Louisville. The Louisville hospitals serve a population of about 400,000 or more. There are nine hospitals for obstetrics and in eight of them cesareans are performed, the other referring its section cases. Louisville, like Cincinnati, has a medical school whose University hospital is the City-County General Hospital where only indigent patients are cared for. Most of the qualified obstetricians of Louisville are members of the teaching staff of the medical school.

During the period of 1950 through 1954, there were about 72,000 deliveries in Louisville. Of these there were 2,179 cesarean sections, an incidence of 3 per cent as compared with 2.41 per cent in Cincinnati. There was a great discrepancy, however, in the various hospital rates. At the General Hospital the incidence was 1.81 per cent, while in the other hospitals the five-year rate varied from 2.23 to 5 per cent. Likewise there was a marked difference in different years, as in one hospital which in 1950 had a cesarean incidence of 10.5 per cent, which gradually decreased each year to 2.79 per cent in 1954.

It is of interest, perhaps, to offer an explanation for some of our contrasting figures. In 1946, the immediate postwar year, there was no regulation of practice in the private hospitals and in at least two of the hospitals cesarean incidence as well as fetal mortality was comparatively high. Beginning in 1946 each department organized, and monthly staff meetings were held in most of the hospitals. Each maternal and neonatal death, cesarean section, direct sterilization, and therapeutic abortion was discussed. These discussions were carried out frankly but impersonally. Almost immediately in those hospitals where there seemed to be too many sections and sterilizations, incidence of these procedures decreased to the generally expected level. It has been the experience in Louisville hospitals that by free and open discussion it is very easy to control substandard practice. Because we are able to accomplish these results at the local level, we resent centralized control in regulating the work in our hospitals.

Consultation is required for all primary cesareans and about 85 per cent of the sections are now performed by obstetricians. Those performed by obstetricians are almost entirely the low segment operation. The cesarean sections performed by general surgeons and practitioners are almost all of the classical type.

Indications for cesareans have not changed very much through the past few years, although a better description of the term "disproportion" as an indication seems to me to be

in order. We are usually taught that disproportion signifies a bony obstruction due to too small a pelvis or too large a baby. Almost always when a section is performed after a trial labor because of so-called disproportion, there are the extenuating circumstances of uterine dyskinesia, sometimes accompanied by malposition and unfavorable cervical effacement and dilatation. The latter indication is seldom mentioned on the record.

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A disturbing factor in fetal mortality and morbidity has been the repeat elective sections performed so early that a premature baby results. Would it not be better policy for patients who had previous cesareans to have beginning labor, and vaginal delivery, to be allowed if progress was satisfactory, rather than arbitrarily to set a date for delivery by cesarean section before the fetus is mature? I realize that many advocate "once a cesarean, always a cesarean," but I personally have delivered successfully many patients vaginally after a previous section.

Over the years there have been claims made that both too few or too many sections are done. As Dr. Bryant so aptly stated, no one regrets having performed the operation, but frequently wishes he had performed a cesarean rather than the vaginal delivery which was not satisfactory. There is no hard-and-fast rule that 3 per cent or 10 per cent or 1 per cent is the proper incidence for cesarean section. The number of unnecessary cesareans will be reduced by the proper discussion and publicizing of such cases among the medical staff. By the same method of discussion of unusual cases and complications, probably certain other patients who have not had the benefit of this operation will have in the future.

DR. L. A. CALKINS, Kansas City, Kan.—I am quite aware of the amount of work that has gone into this contribution as I had, many years ago, the assignment of analyzing all the cesarean sections done by the members of the Central Association of Obstetricians and Gynecologists in one year. Dr. Bryant has been very careful, perhaps overly zealous, not to criticize indications, technique, or results. He has, very definitely, avoided the attitude of the reformer.

A rate of 2,486 cesarean sections in more than 100,000 pregnancies is certainly not high. As compared to the rate in most series, it is low. When we realize, however, that most of the reports come from hospitals to which a considerable number of patients are referred, and Dr. Bryant's figures are from a community to which only a small percentage of the whole number of patients could have been referred, his figures probably come closer to the cross section of modern-day practice. As such, it may be a good figure with which to compare one's own nonreferred practice.

Two hundred thirty-four sections were done for placenta previa, and only 143 for premature separation of the placenta. In view of the much higher relative incidence of the latter condition, this represents a laudably conservative attitude of the Cincinnati profession toward premature separation. Indications, in general, were apparently honestly stated. I am told by Dr. Bryant that such indications as "DDS-6", "Post-mature—3" (these have not read Calkins' article), "Ruptured Membranes—8" (neither have these), "Extravaluable Baby—3" (I believe all babies are extravaluable) were offered by obstetricians. The general practitioners cannot, therefore, be blamed on this score. An 80 per cent salvage of babies when cesarean section was done for prolapsed cord is a very encouraging report, indeed.

The morbidity figures are good—perhaps too good—when one considers the large number of physicians concerned. The same is not quite true of the mortality figures. Eleven mothers were lost. True, 8 of these would probably have died anyway. Was the fetal salvage (as previously pointed out by Fred Falls and others) sufficiently high to justify an untimely death? Dr. Bryant tells me that 7 of these babies survived. Certainly, that is a much better record than anyone, to my knowledge, has reported from so-called "postmortem cesarean section." None of the other 4 could be expected to survive at the time the sections were done. The section on the patient with carcinomatosis could very well have been delayed several weeks, as she did not die till many months later.

There were 87 babies stillborn and 103 died in the neonatal period, a total of 7.6 per cent for the perinatal mortality. This figure corroborates the opinion of Plass and others that cesarean section is not, necessarily, the "ideal" way for a baby to be born. I could not tell from Dr. Bryant's paper whether the cesarean section had been so long delayed that the 103 babies who died in the neonatal period had been too much damaged before interference. I presumed that the 87 sections resulting in stillborn babies were done for maternal indications.

Eleven mothers (a figure which could be "corrected" to 3) and 190 babies is a considerable loss. Cesarean section is not yet completely safe even when 82 per cent of the operations are done by specialists. It seems worth while to continue to study indications carefully, and, as Edward Schumann has pointed out, to consider very carefully the timing of the operation.

DR. J. P. GREENHILL, Chicago, Ill.—I agree with Starr that in most elective sections we should preferably wait until the onset of labor or spontaneous rupture of the membranes. In the series of cesarean sections reviewed by Bryant 65 patients were listed as having had disproportion and yet elective operations were done. I do not think we are justified in saying that a patient has disproportion without having given her some test of labor except in rare cases, such as the presence of hydrocephalus or severe degrees of pelvic contraction or distortion. All of us have seen patients on whom we thought we might have to do a cesarean section, yet Nature, by combined efficient uterine action and molding of the baby's head, produced live healthy babies without damage to them or the mothers. I believe 65 cases of elective cesarean section for disproportion without test of labor are far too many.

The matter of fetal deaths in placenta previa is very important. Those of you who will stay over until tomorrow will hear Robert Johnston speak specifically about that question and my discussion of this subject.

In closing, I should like to emphasize one point brought out, namely, the definition of cesarean section. I fully agree that an operation on a patient with a ruptured uterus should not be listed as a cesarean section.

DR. BRYANT (Closing).—The statistics from Louisville are extremely interesting, and roughly parallel with those in Cincinnati, I believe.

Dr. Calkins obviously went over the full text of the paper word by word, and made some very interesting observations. This material was compiled not with the idea of criticizing anybody, but rather of determining exactly what the situation in a community is. None of these were postmortem cesarean sections.

As for allowing the onset of labor before a cesarean section is performed, this is done sometimes in Cincinnati. The objection to it, in our community, is the fact that in a majority of the hospitals the general operating rooms must be used, so that if patients who have previously had a cesarean section are admitted in labor between 7 A.M. and noon, there may be a delay of several hours before an operating room may be secured. As pointed out in the paper, 5.4 per cent of the babies delivered by elective section were premature by weight. There may be a fallacy here, however, because if you do an elective section two weeks prior to term and deliver a 5 pound, 7½ ounce baby, it is, by definition, premature. Actually, however, if that baby had been allowed to go to full term it might have weighed over 6 pounds.

The elective sections for disproportion are described in the formal part of the paper. I was surprised myself that there were that many because everyone says, "I've never done an elective section for disproportion, they always have to go into labor," yet there were 65 patients in whom it was done. Several of the elective sections for disproportion were in patients whose babies had hydrocephalus.

CLINICAL PROBLEMS IN STAGE 0 (INTRAEPITHELIAL) CANCER OF THE CERVIX*

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IN 1952, our group¹ reported on the management and follow-up of 151 patients with intraepithelial cancer of the cervix (Stage 0). That report covered a five-year period from Jan. 1, 1947, through Dec. 31, 1951, and gave a factual account of our methods of diagnosis and treatment. We gave also the results of two questionnaires which were sent to gynecologists and pathologists concerning their attitudes to cancer in situ of the cervix and asking for their suggestions on methods of therapy.

The present report is a follow-up on the 151 patients previously studied, augmented by the patients with intraepithelial cancer who were studied and treated from Jan. 1, 1952, through June 30, 1955. This study covers a period of eight and one-half years and reports on a total of 275 patients with Stage 0, squamous-cell cancer.

The purposes of this report are:

- 1. To give the picture of Stage 0 cancer in relation to the problems of cancer of the female generative tract as a whole and to show how we have met these problems in the last eight and one-half years.
- 2. To present the clinical data on these 275 patients with Stage 0 cancer of the cervix.
- 3. To criticize some of our previous therapeutic operative methods and to give the clinical courses of those patients who are being followed under "conservative" therapy or after some type of "definitive" treatment.
- 4. To discuss some of the problems which perturb us as well as some of our colleagues in the other medical specialities, as we work conjointly on the problems of Stage 0 cancer of the cervix.
- 5. To emphasize, again, that obstetric patients should not be denied, with casualness, the benefits of routine screening by cytologic techniques. This procedure is essential for the frequent detection and diagnosis of Stage 0 cancer. It is our feeling that all females who enroll in our clinic, of whatever age, parity, or race, should have a systematized search for cancer.

No attempt is made in this report to review the historical literature or to cover the more recent voluminous reports of intraepithelial cancer.

^{*}Presented at the Sixty-sixth Annual Meeting of the American Association of Obstetricians and Gynecologists, Hot springs, Va., Sept. 8 to 10, 1955.

We feel that the criteria used by our Department of Pathology to establish the diagnosis of intraepithelial carcinoma are adequate and conservative.

We draw no conclusions from this small series of patients, because we realize that our data are not yet of statistical significance.

Clinical Material

Table I summarizes briefly certain data on patients with intraepithelial and with invasive squamous-cell cancer studied by cytologic and histopathologic techniques from Jan. 1, 1947, through June 30, 1955, a period of eight and one-half years. This table shows the necessity for including in these diagnostic procedures the obstetric as well as the gynecologic patients. The incidence of Stage 0 cancer in the obstetric patients was 0.57 per cent; in the gynecologic patients the incidence was 0.58 per cent. These almost identical figures are of interest in regard to the etiology of this lesion in pregnancy.

Table I. Intraepithelial and Invasive Squamous-Cell Carcinoma Studied, Jan. 1, 1947, Through June 30, 1955

	OBSTETRIC 6,5		GYNECOLOGIC PATIENTS 40,739*	
	NONINVASIVE INTRAEPITHELIAL CA. OF CERVIX	INVASIVE SQUAMOUS-CELL CA. OF CERVIX	NONINVASIVE INTRAEPITHELIAL CA. OF CERVIX	INVASIVE SQUAMOUS-CELL CA. OF CERVIX
No. of Patients	_			
White	22	9.	182	477
Negro	16	12	55	451
Total	38	21	237	928
Incidence	0.57%	0.32%	0.58%	2.28%
Average Ages.—				
White	30.2 years	31.9 years	40.5 years	49.2 years
Negro	29.1 years	33.8 years	37.5 years	48.7 years
Combined	29.8 years	33.0 years	39.8 years	48.9 years

^{*}Approximate.

The higher incidence, 0.84 per cent, for in situ cancer in obstetric patients, as previously reported by us, was due to a combination of selective and incomplete cytologic screening of pregnant patients.

It is our feeling that the detection of intraepithelial carcinoma is a departmental problem rather than that of any one or two individuals. When proper screening and diagnostic techniques are used as a routine in the care of the individual patient, the number of these neoplasms found will be increased in every clinic.

Table II gives data on the patients studied by cytologic and histopathologic techniques during the same eight and one-half years, who were proved by pathologic diagnosis to have some type of genital malignancy.

The last column gives the percentage error for the cytologic screening of these patients with the more common types of genital malignancies. These percentage errors should not be magnified as an argument against the use of exfoliative cytology. These percentage errors represent the uncorrected reports on the first set of exfoliative cytologic smears studied for each patient. The verification column does not signify that the type and primary site of malignancy were recognized correctly on each set of smears. It means simply that malignancy was recognized in the exfoliative cytologic studies. Ovarian cancers are listed in this table usually when involvement of the lower genital tract resulted in the exfoliation of cells recoverable by cytologic techniques.

A study of Tables I and II will show clearly the problem of Stage 0 cancer in relation to genital cancers in general.

Table II. Malignancies Studied by Genital Smears, Jan. 1, 1947, Through June 30, 1955.

Total Number of Patients Studied 47,239

Total Number of Smears Studied 176,773

TYPES OF MALIGNANCY	MALIGNANT BY SMEAR AND PATH. (VERIFIED)	MALIGNANT BY PATH. ONLY (MISSED)	TOTAL	% ERROR
Squamous cell carcinoma	(VERIFIED)	(MISSED)	TOTAL	Ention
Cervix	864	85	949	8.9
Vulva	38	11	49	22.4
Vagina	16	2	18	11.1
Origin undetermined (in vagina)	1	2	1	11.1
Urethral meatus	2		2	
Adenoacanthoma	2		2	
Cervix	3	1	4	25.0
Endometrium	5	11	16	68.7
Adenocarcinoma	ð	11	10	00.7
Cervix	40	5	45	11.1
Endometrium	89	42	131	32.1
Oviduct		42	2	32.1
	2		4	
Origin unknown (in uterus or vagina)	4	0	19	
Ovary, metastatic	17	2		
Intestine, metastatic	2	0	2	
Rectum, metastatic	6	3	9	
Krukenberg tumor	1		1	
Granulosa-cell, metastatic	2		2	
Chorionepithelioma	2	1	3	
Teratoma of uterus	1		1	
Dysgerminoma, metastatic		1	1	
Carcinosarcoma, endometrium	1		1	
Sarcoma				
Uterus	4	2	6	
Leiomyosarcoma	2		2	
Rhabdomyosarcoma	1		1	
In myomatous transformation		2	2	
Vaginal wall	1		1	
Botryoides	1		1	
Hemangiosarcoma		1	1	
Basal-cell carcinoma, vulva	3		3	
Undifferentiated carcinoma				
Endometrium	1		1	
Metastatic	3	2	5	
Carcinoma in cervix, origin unknown		1	1	
Total	1,112	172	1,284	

Table III compares the incidence in age groups of intraepithelial and invasive squamous-cell cancer of the cervix. It shows the age distribution in five-year age groups, the number of patients in each age group, and the percentage of the total number of lesions each age group represents.

The average age for patients with Stage 0 cancer was 38.4 years; the youngest patient was 19 years of age, the oldest patient was 80 years of age. The average age of the 151 patients reported previously was also 38.4 years.

The average age for patients with invasive cancer was 48.6 years; the youngest patient was 21 years of age and the oldest patient was 85 years of age. The average age of the 566 patients reported previously was 48.0 years.

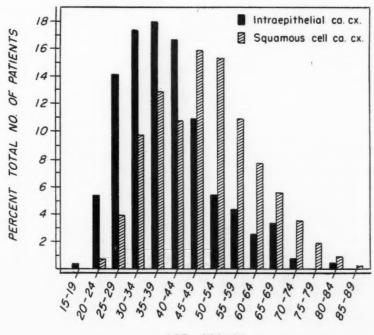
Table IV, in graph form, shows the incidence of intraepithelial and of invasive cancer in per cent of the total number of patients and by five-year age groups.

Table V presents the race and the economic status of the 275 patients with intraepithelial cancer of the cervix.

Table III. Age Incidence of Squamous Carcinoma of the Cervix, Jan. 1, 1947, Through June 30, 1955

	INTRAEPI (27		INVASIVE (949)		
AGE GROUP	NO. PATIENTS	% OF TOTAL	NO. PATIENTS	% OF TOTAL	
15-19	1	0.4			
20-24	15	5.4	7	0.7	
25-29	39	14.2	37	3.9	
30-34	48	17.5	92	9.7	
35-39	50	18.2	123	12.9	
40-44	46	16.7	103	10.8	
45-49	30	10.9	152	16.0	
50-54	15	5.4	144	15.4	
55-59	12	4.4	103	10.9	
60-64	7	2.5	73	7.7	
65-69	9	3.3	53	5.6	
70-74	2	0.7	34	3.5	
75-79			18	1.9	
80-84	1	0.4	9	0.9	
85-89			1	0.1	
Average age Age range	38.4 years 19-80		48.6		

Table IV. Patients With Intraepithelial Carcinoma and Invasive Squamous-Cell Carcinoma of the Cervix Presented by Five-Year Age Groups and in Per Cent of Total, Jan. 1, 1947, Through June 30, 1955.



AGE GROUPS

TABLE V. RACE AND ECONOMIC STATUS

	JAN. 1, 1947, THROUGH DEC. 31, 1951			JAN. 1, 1947, THROUGH JUNE 30, 19			
RACE	PRIVATE	CLINIC	TOTAL	PRIVATE	CLINIC	TOTAL	
White	61	44	105	119	85	204	
Negro	8	38	46	9	62	71	
Total	69	82	151	128	147	275	

Table VI shows the marital status of the 275 patients with intraepithelial cancer of the cervix.

TABLE VI. MARITAL STATUS

MARITAL STATUS	JAN. 1, 1947, THROUGH DEC. 31, 19511	JAN. 1, 1947, THROUGH JUNE 30, 1955
Single	4	5
Married	125	221
Widowed	10	16
Separated	9	. 31
Unknown	3	2
Total	151	275

Table VII gives the parity of the 275 patients with intraepithelial cancer of the cervix.

TABLE VII. PARITY

PARITY	JAN. 1, 1947, THROUGH DEC. 31, 1951 ¹	JAN. 1, 1947, THROUGH JUNE 30, 1955
Nullipara	21	26
Unipara	23	50
Multipara (2-4)	61	131
Multipara (5+)	35	60
Unknown	11	8
Total	151	275

TABLE VIII. CLINICAL IMPRESSION OF CERVICES

IMPRESSION		JAN. 1, 1947, THROUGH DEC. 31, 1951		JAN. 1, 1947, THROUGH JUNE 30, 1955		
		NO.	% OF TOTAL	NO.	% OF TOTAL	
Clean and healthy		26	19.8	47	19.8	
Cervicitis		85	64.9 Benign	153	64.5 Benign	
Leukoplakia		4	3.1	10	4.2	
Questionable malignancy Cervical?	10	13	9.9	22	9.3	
Endometrial?	3		12.2	1	11.5	
Ovarian?	0		Malig.	1	Malig.	
Squamous-cell carcinoma		3	2.3	5	2.2	
No comment or unknown		20		38		
Total	-	151		275		

Table VIII gives the data for 217 patients, from the total of 275 patients, with intraepithelial cancer of the cervix, upon whom a definite clinical impression of the cervix was written into the patient's record when the patient was first examined. It has been a Departmental teaching policy that emphasis be placed on a clinical assessment of the cervix. Despite this, it is evident that after eight and one-half years, the examiners are no more adept in recognizing cervices which harbored in situ lesions than they were at the end of the first five-year period. In the five years, 1947 through 1951, the clinical examiners of 131 patients with Stage 0 cancer of the cervix considered the cervix "benign" in 87.8 per cent and "malignant" or "questionably malignant" in but 12.2 per cent. In the eight and one-half years these figures were 88.5 per cent "benign" and 11.5 per cent "malignant" or "questionably malignant" for the total of 217 patients. These facts illustrate the obligation to screen all female patients by exfoliative cytologic techniques.

Table IX lists the operative procedures which provided tissue for the pathologists' studies and diagnoses for the 275 patients with intraepithelial cancer of the cervix.

TABLE IX. OPERATIVE PROCEDURE WHICH PROVIDED TISSUE FOR DIAGNOSIS

	NO. OF PATIENTS			
OPERATIVE PROCEDURE	JAN. 1, 1947, THROUGH JUNE 30, 1955	JAN. 1, 1947, THROUGH DEC. 31, 1951		
Multiple punch biopsy, one occasion	128	88		
Multiple punch biopsy, two or more occasions	13	13		
Full thickness wedge; had previous punch	1	1		
Cold-knife conization 23 patients had previous punch biopsy 4 patients had two previous punch biopsies 2 patients had three previous punch biopsies	108	37		
Vaginal removal of cervical stump	4	2		
Total hysterectomy 7 patients had previous punch biopsy 1 patient had three previous punch biopsies and cold-knife conization 1 patient had previous cold-knife conization	21	10		
Total	275	151		

Even though multiple punch biopsies are not the ideal methods for securing adequate specimens for pathologic diagnoses, they cannot be discarded from clinic practice at the present time and under existing economic and social conditions. It is mandatory, however, to insist that no reliance be placed on punch biopsies when the pathologists' studies fail to show intraepithelial carcinoma or do not demonstrate invasion in the presence of intraepithelial cancer. Should the exfoliative cytologic studies continue to show anaplastic cells, then conization with a cold knife should be done. When intraepithelial carcinoma only is shown in pathologic study of punch biopsy material, a cold-knife conization is necessary to provide adequate tissue to try to exclude invasive cancer.

Cold-knife conization of the cervix should be done as a hospital procedure. When an adequate cone specimen is secured, suturing of the cervix for hemostasis should be done. The proper techniques for securing the cone, without trauma to the epithelia of the portio or of the endocervix, should be fully understood.

In our clinic the chief value of the punch biopsy is to diagnose invasive carcinoma in a clinically suspicious or cytologically abnormal cervix. If invasion can be proved by this clinic procedure, the patient is saved delay in diagnosis and in treatment and the expense of hospitalization for the cold-knife conization.

Table X lists the treatment of the 237 gynecologic patients with intraepithelial cancer of the cervix.

It should be noted that 10 patients (2.4 per cent) had in situ cancer in the cervical stump. We have adopted the practice of total vaginal removal of these cervical stumps with wide vaginal cuffs.

In the total of 237 gynecologic patients with Stage 0 cancer of the cervix, there are 57 patients upon whom no further definitive procedures have been done other than multiple punch biopsies (7 patients) and cold-knife cone biopsies (50 patients).

In the critical analysis of the therapy of these 237 patients, we feel that vaginal hysterectomy with removal of a wide margin of vaginal cuff is preferable to abdominal hysterectomy, as was practiced more commonly in the

earlier years of this study. We feel also that we were too radical in removing the ovaries, in the age groups from 20 to 39 years, at the time of vaginal or abdominal hysterectomy.

TABLE X. GYNECOLOGIC PATIENTS

TREATMENT	AGE GROUP	NO OF	PATIENTS	FOCI OF INVASION
Multiple punch biopsy	20-29	1	***********	11111110101
1 1	40-49	3		
	50-59	2		
	60-69	1	7 '	
Cold-knife conization of cervix	10-19	1	,	
	20-29	15		
	30-39	25		
	$40-49 \\ 50-59$	$\frac{3}{1}$		
	60-69	3		
	70-79	1		
	80-89	1	50	
Vaginal removal of stump	37-57	10	10	1
Amputation of cervix, elsewhere	37	1	1	
X-ray, elsewhere	50-60	3	. 3	
Radium and x-ray	57	1	1	
Radium	44	1	1	
Radium, elsewhere	45-56	3	3	
Treatment unknown, elsewhere	27	1	1	
Vaginal hysterectomy, conservation of ovaries	20-29	9		
	30-39 40-49	20 19		
	50-59	5		
	60-69	5		
	70-79	1	50	
Vaginal hysterectomy, bilateral salpingo-	20-29	1	59	
oophorectomy, bhaterar sarpingo	30-39	2		
,	50-59	2		1
	60-69	1	0	
Panhysterectomy, conservation of ovaries	20-29	5	6	
Fannysterectomy, conservation of ovaries	30-39	20		2
	40-49	8		1
	00.00	0	33	
Panhysterectomy, bilateral salpingo-oophorectomy	$20-29 \\ 30-39$. 7		
	40-49	29		
	50-59	11		
	60-69	4		1
Radical hysterectomy, bilateral salpingo- oophorectomy*		5*	53	
Radical hysterectomy, bilateral salpingo-oophor- ectomy and bilateral pelvic lymphadenectomy	60-69	1	1	
Panhysterectomy, elsewhere	20-29	1		
2 ming storousing, order note	30-39	4		
	40-49	3		
			8	
lotal			237	6

^{*}Prior to, and not counted in, this series.

Discrepancies between the total figures for certain categories in the "Treatment Table" X in this report and those in the "Treatment Tables" IX and X in the original 1952 report are due to elimination from this series of a number of patients treated and followed elsewhere (uncontrolled or lost).

Six examples of microscopic foci of invasion were found on study of multiple block sections of the specimens obtained from these 237 gynecologic patients. As stated in the 1952 report, these patients constitute an interesting group for follow-up. To the present date none of the 6 has shown clinical invasive cancer or suspicious exfoliated cells.

If all biopsy specimens could be subjected to multiple block sectioning, we believe that microscopic foci of invasion, or possibly invasive cancer, might be found in a greater number of specimens.

Table XI gives the treatment of 38 obstetric patients with Stage 0 cancer of the cervix.

TABLE XI. OBSTETRIC PATIENTS

TREATMENT	NO. OF PATIENTS	FOLLOW-UP DATA
Multiple punch biopsy	10*	4 have not returned since establishment of diagnosis 1 patient is now pregnant 1 patient died in uremia with eclampsia 4 patients are being followed
Cold-knife conization of cervix	11*	1 patients are being followed 1 patients are being followed
Vaginal hysterectomy, conservation of ovaries	12	T
Panhysterectomy, conservation of ovaries	3	1 patient had microscopic foci of in- vasion
Panhysterectomy, bilateral salpingo- oophorectomy	2	
Total	. 38	

^{*}See Table XIII regarding subsequent pregnancies in these patients.

It is interesting to note that one patient in this group had microscopic foci of invasion found in multiple block sections. This patient was treated by panhysterectomy with conservation of the ovaries. To date, there has been no further evidence of either intraepithelial or invasive cancer.

We feel that the same cytologic and pathologic techniques should be used for the obstetric patients as for the gynecologic patients.

Pregnancy in the younger age groups is the time for education of the female for subsequent care.

Table XII gives the data on 7 of the 237 gynecologic patients who became pregnant subsequent to the diagnosis of Stage 0 cancer of the cervix.

TABLE XII. PREGNANCIES SUBSEQUENT TO DIAGNOSIS IN 7 OF THE 237 GYNECOLOGIC PATIENTS

PATIENT	AGE*	NO. OF LIVING CHILDREN*	EXTENT OF SURGICAL PROCEDURE*	NUMBER OF PREGNANCIES	DEFINITIVE THERAPY
1. E. H.	27	0	Cold-knife conization	1 tubal	Yes
2. E. F.	24	2	Cold-knife conization	2	No
3. N. S.	31	3	Cold-knife conization	2	Now pregnant
4. E. H.	27	0	Multiple punch biopsyt	1	No
5. J. W.	39	3	Cold-knife conization	1	No
6. V. S.	30	1	Cold-knife conization	1	No
7. S. A.	24	2	Cold-knife conization	1	No

^{*}At time of subsequent pregnancy.

[†]Only patient in whose genital smears atypicalities persist and only patient who had multiple punch biopsy.

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It may be significant that the 6 patients who had a cold-knife conization of the cervix have not continued to show atypicalities in their genital smears. The one patient of these 7 who continues to have atypicalities in her smear preparations was the patient upon whom multiple punch biopsy alone was done.

Table XIII presents data on 11 of the 38 obstetric patients with Stage 0 cancer of the cervix who became pregnant subsequent to the diagnosis.

TABLE XIII. PREGNANCIES SUBSEQUENT TO DIAGNOSIS IN 11 OF THE 38 OBSTETRIC PATIENTS

PATIENT	AGE*	NO. OF LIVING CHILDREN*	EXTENT OF SURGICAL PROCEDURE*†	NO. OF SUBSEQUENT PREGNANCIES	DEFINITIVE THERAPY
1. A. B.	25	3	Multiple punch biopsy	1	Yes
2. A. P.	35	4	Multiple punch biopsy	1	Yes
3. M. H.	39	2	Multiple punch biopsy	2, 1 tubal	No
4. L. C.	24	2	Multiple punch biopsy;	1	No
5. A. H.	27	1	Multiple punch biopsy	1	No
6. J. F.	26	2	Cold-knife conization	2	No
7. M. D.	23	3	Multiple punch biopsy	1	No
8. I. B.	32	1	Cold-knife conization	1	Yes
9. R. H.	25	3	Cold-knife conization	1 abortion	No
10. B. J.	28	0	Cold-knife conization	2 abortions	No
11. E. C.	31	2	Multiple punch biopsy;	2	No

*At time of subsequent pregnancy.

†Not necessarily the diagnostic procedure.

‡Patients in whose genital smears atypicalities persist.

Three patients (Nos. 1, 2, and 8) have had definitive treatment at the time of this report. Two of these 3 patients were permitted to go through one pregnancy before definitive treatment was given. Eight patients who have not had definitive therapy are being followed.

Mortality.—There has been one operative death following vaginal hysterectomy as definitive treatment for Stage 0 cervical cancer. The patient was a poor operative risk with marked obesity and with hypertensive cardiovascular disease.

Complications.—There have been no complications noted as the result of operations for diagnosis or for definitive treatment other than the operative death mentioned. Several patients upon whom cold-knife cone biopsy was done had to have the cervix resutured for hemostasis. Cervical stenosis has not been a problem and is readily controlled by routine soundings of the cervix.

Psychic Effects.—In this series of 275 patients, one patient had a depressive psychosis prior to the diagnosis and treatment of Stage 0 cancer of the cervix and later committed suicide despite psychiatric care. We did not feel that her death could be attributed to the diagnosis and definitive treatment of intraepithelial carcinoma.

Drug Addiction.—No patient in this series has developed drug addiction.

"Follow-Up" on Patients

The follow-up is the most important feature of any program for Stage 0 cancer of the cervix or of the cervical stump. For those patients who have had only conservative treatment, it is absolutely essential that all techniques for adequate follow-up be used. For those who have had what is termed definitive treatment, the follow-up is of equal importance if we are to learn more concerning what intraepithelial cancer really means to patients and to us. Anyone who elects to treat the lesion by either the conservative or the definitive approach assumes a definite obligation to the patient. Many terms

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still must be defined. The pooling of information from many clinics must be expedited if we are to clarify the confusion which now exists in the criteria both for diagnosis and for the methods of treatment.

Data are presented in Table XIV to illustrate the frequency of follow-up visits in 78 patients, 57 gynecologic and 21 obstetric, with Stage 0 cancer of the cervix. Diagnoses were established by multiple punch biopsies and cold-knife cervical conizations. The patients have not yet had definitive therapy. Five of these patients have not returned since their diagnoses were established. These are considered lost to our program. There have been no follow-up studies on 13 patients on whom there have been recent diagnostic procedures. The remaining 60 are tabulated according to the number of follow-up visits made per patient, the number of patients in each category, and the total number of follow-up visits for each category.

TABLE XIV. FOLLOW-UP

NO. OF FOLLOW-UP VISITS PER PATIENT	NO. OF PATIENTS	TOTAL NO. OF FOLLOW-UP VISITS	
1	10	10	
2	9	18	
3	6	18	
4	7	28	
5	9	45	
6	4	24	
7	5	35	
8	1	8	
9	0	0	
10	4	40	
11	1	11	
12	2	24	
13	0	0	
14	2	28	
Total	60	289	

These same 60 patients are grouped in Table XV according to the duration, in years, of their follow-up periods.

TABLE XV. DURATION OF FOLLOW-UP

NO. OF PATIENTS	DURATION IN YEARS
12	(2 to 10 months)
22	1
9	2
9	3
4	4
3	5
1	6
Total 60	

The duration of the follow-up period extends from the date of diagnosis to the date of the last follow-up visit.

No patient included in the present series who has had definitive treatment for Stage 0 cancer shows persistent atypicalities in genital smears. Three gynecologic patients, one who had multiple punch biopsies and 2 who had cold-knife conizations, continue to show cytologic atypiae in their smears. Two of these patients desire more children. One patient, who has had a cervical conization, is 74 years of age and has severe cardiovascular disease. Two obstetric patients, who have had but multiple punch biopsies, have persistent atypical cervical epithelium in genital smears. Each patient was recently delivered.

Progress From Stage 0 to Invasive Cancer.—To our knowledge, none of the patients who are now being followed without definitive treatment, has developed invasive squamous-cell cancer of the cervix.

The Problems Associated With Stage 0 Cancer of the Cervix Involve Colleagues in Many Hospital Specialties

The problems which arise in any consideration of Stage 0 squamous-cell cancer of the cervix are legion and involve many of the specialties of hospital technical practice. Among those concerned with the problems are the gynecologist and obstetrician, the patient, the cytologist, the pathologist, the

The Clinician.—The clinician must understand the necessity for the patient's comprehension of the potentialities of intraepithelial cancer of the cervix. He must be willing to institute proper techniques for adequate genital smears for the cytologist and proper biopsy specimens for the pathologist. He must realize the limitations, as well as the potentialities, of exfoliative cytology in the hands of competent cytologists. The clinician should not accept cytologic reports labeled "positive," "doubtful," or "negative," but should demand more detailed information. He must know the thoroughness of the pathologic studies done on any piece of tissue submitted by him to the pathologist for analysis. He should have confidence in the pathologist's reports as regards the concepts of the pathologist in the consideration of this lesion. He should also ascertain the degree of adequacy of the studies upon which the pathology report is based. The clinician should realize that his treatment of the lesion must be individualized. Even though he accepts Stage 0 in his concept of cancer of the cervix he must realize that it is an entity whose possibilities and vagaries are as yet poorly understood.

The Patient.—The patient should not be "terrorized" by the diagnosis of intraepithelial cancer of the cervix. She should not be given a false sense of security by conclusions reached by either screening or diagnostic techniques, or by therapeutic measures. When any form of conservative treatment is contemplated by the clinician the patient must be made to understand the potentialities of the lesion. She must appreciate the necessity for the screening and for the diagnostic techniques which must be applied to her. She must be able to cooperate fully with the group which will attempt to get a definitive diagnosis, and from this diagnosis will plan individualized, definitive therapy. Failure of the patient to understand the entire situation may lead to confusion and misunderstanding in the therapeutic approach or to inadequate treatment. The patient must realize that follow-up is mandatory.

The Cytologist.—The cytologist must have a training and an experience which are totally adequate. He must be familiar with the associated clinical pathologist's concept of, and criteria for, intraepithelial cancer. He must be able to alter, if necessary, criteria used in his laboratory to conform to the criteria of the contemporary pathologist. He must be conservative and accurate, to minimize the possible psychic effects on patients of a suggestion of cancer of whatever staging. His accuracy and experience should be expressed in an ability to differentiate frequently between noninvasive and invasive lesions. He must not make diagnostic interpretations from smear preparations which are of poor quality or which obviously do not represent the areas involved by the lesion.

The cytologist must constantly teach the proper techniques for obtaining good smears. He must stress the fact that poor smears are due primarily to: (1) careless techniques; (2) poor or delayed fixation; (3) too few epithelial cells in the smears due to the first two factors. In our clinic a large

number of Stage 0 cancers would have been missed had not material been obtained from deep in the endocervical canal by aspiration before and after sounding of the endocervix.

The Pathologist.—The clinician's attitude toward this lesion depends upon the pathologist and his concepts of intraepithelial cancer. The pathologist must accept intraepithelial cancer of the cervix as an entity and must be interested in the problems it causes. He must insist upon adequate tissues for his studies. He must demand biopsy specimens which have been obtained by techniques which do not denude the portio of the cervix or the endocervix of their epithelia. He must also institute adequate studies of the tissues submitted to him, even though these studies are costly and time consuming. He should have sufficient funds and well-trained technical helpers to further the studies of multiple block sections. He must teach that inadequate tissue and inadequate study of adequate tissues may result in the underdiagnosis of intraepithelial and invasive cancer.

The pathologist must use his influence: (1) to combat a feeling of false security in either patient or clinician; (2) to decrease delay in the definitive diagnosis and in definitive treatment. He must also help to establish in the clinician confidence in the work of the cytologist as well as in that of the pathologist. His criteria for the diagnosis of intraepithelial cancer should be understood by the clinician and by the cytologist. The cytologist's criteria for "screening" certain patients into groups requiring adequate biopsy studies also should be fully appreciated by the pathologist.

In short, the professional and intellectual capacity of the pathologist is, in effect, the first cornerstone for building a firm foundation for a possible understanding of Stage 0 cancer of the cervix.

The Endocrinologist.—The interest of the endocrinologist in the problem of Stage 0 squamous-cell cancer of the cervix should be encouraged. There are some who believe that "hormones" may cause changes in the epithelium of the female genital tract which may predispose to the development of epithelial atypicalities. It is well known that many observers will not accept the diagnosis of Stage 0 cancer of the cervix during pregnancy; that others believe "regression" of Stage 0 cancer can occur spontaneously or under certain hormonal therapy, in both nonpregnant and pregnant individuals. If it is logical to accept intraepithelial cancer as a disease of the cervix or endocervix, it would seem logical to accept it also as a disease of the vulva, vagina, and endometrium. The part which the endocrinologist could play in the study of Stage 0 cancer should be broadened in all studies of the lesion.

The Roentgenologist.—In the therapy of cancer, the roentgenologist plays a major role in this and in other countries. His interest in, and knowledge of, the effects of irradiation on the tissues of the generative tract should include a true interest and a wide knowledge of Stage 0 cancer of the cervix. He must decide, after reviewing his concept of this lesion, whether he would treat Stage 0 cancer with irradiation therapy or whether he would elect to have it treated by operative methods. His ideas should be considered by all of us in our attempt to determine what is the best treatment for the patient with a Stage 0 lesion.

The Psychiatrist.—The campaign to educate "the public" in cancer-control methodology has led to many fears in all age groups of our female population. The cancer phobias, the mental attitudes of patients in accepting any diagnosis of cancer from Stage 0 to Stage V, the reaction of patients to any given method of treatment, and the mental reactions which may follow any form of therapy for tumors or cancers of the generative tract are but a few of the problems with which all of us are familiar. The psychiatrist has

to help in many of these situations when our own clinical psychiatric efforts fall short or fail in accomplishing our goal. We would be better prepared if we had more psychiatric data on the reaction of patients to our diagnosis and treatment of all stages of cervical cancer.

Squamous-Cell Cancer of the Vagina Diagnosed After Definitive Diagnosis and Definitive Treatment for Stage 0 Cancer of the Cervix

Two patients had a diagnosis of invasive squamous-cell cancer of the vagina after definitive diagnosis and definitive therapy for intraepithelial carcinoma of the cervix. A brief outline is given for each.

1. Patient T. S., C-95346, a 75-year-old Negro woman, gravida xi, with 6 living children and 2 abortions, was seen in the Out-Patient Clinic on Aug. 30, 1950, because of postmenopausal bleeding and a myomatous uterus. Cytologic smears indicated invasive squamous-cell cancer. On Sept. 1, 1950, a fractional dilatation and curettage and biopsies of cervix and endocervix were done. The pathologist's report was probable intraepithelial cancer of the cervix. No invasive cancer was found. On Sept. 7, 1950, total abdominal hysteromyomectomy and bilateral salpingo-oophorectomy were done. The pathologist's report was intraepithelial cancer of the cervix with extension into the endometrium. No invasive cancer was found although many sections from many blocks were studied. The patient, despite instructions, did not return to the clinic until June 22, 1952. At this visit cytologic smears indicated invasive cancer in the vaginal cuff (Fig. 1). The patient refused to have a radical operation for cancer of the vagina. Irradiation therapy was given. The patient died of cancer in October, 1953.

2. Patient T. G., D-4848, a 41-year-old white married woman, para iv, with 3 living children and no abortions, was seen in a State Cancer Detection Clinic in December, 1950. Genital cytology was reported as suspicious and cervical biopsy was reported as intraepithelial cancer. The patient was first seen in our Out-Patient Clinic on Jan. 15, 1951.

Jan. 15, 1951: The cervix was normal in size, mobile, firm, and had erosion of the anterior lip which bled to the touch. The genital cytology was thought to represent squamous-cell cancer. Biopsy of the cervix showed intraepithelial cancer.

Jan. 18, 1951: Cold-knife conization of the cervix and dilatation and curettage were performed. The pathology report was intraepithelial cancer.

March 5, 1951: Cytologic studies were thought to represent squamous-cell cancer but possibly only intraepithelial cancer.

March 7, 1951: Vaginal hysterectomy was done. The final pathologic diagnosis, on 20 blocks of cervical tissue studied, was intraepithelial cancer with no evidence of invasion.

Aug. 20, 1951: The vaginal walls were clean and the cuff was well healed. Cytologic studies indicated intraepithelial cancer.

Oct. 6, 1951: Genital cytology was unchanged. A biopsy of the vaginal cuff showed only granulation tissue.

Oct. 6, 1951, to Nov. 16, 1953: Numerous cytologic studies indicated either intraepithelial cancer or invasive cancer. Biopsies from the cuff and from the vaginal mucosa were reported as cancer in situ and invasive cancer in isolated areas in the vaginal mucosa.

Jan. 18, 1954: Thirty full-thickness biopsies of the vaginal wall were obtained. The pathologic diagnosis on this material was hyperplasia of the vaginal mucosa.

Sept. 20, 1954: Genital cytology showed intraepithelial cancer or invasive cancer. Jan. 24, 1955: The genital cytology was unchanged. Thirty-three biopsies from the cuff and vagina were taken. There was no microscopic evidence of either intraepithelial cancer or of invasive cancer in any of the tissues studied.

July 18, 1955: Interval cytologic smears continued to show neoplastic cells. A partial colpectomy with removal of all of the mucosa of the upper vagina was done. Pathologic analysis of this tissue was reported as invasive cancer of the vagina (Fig. 2).

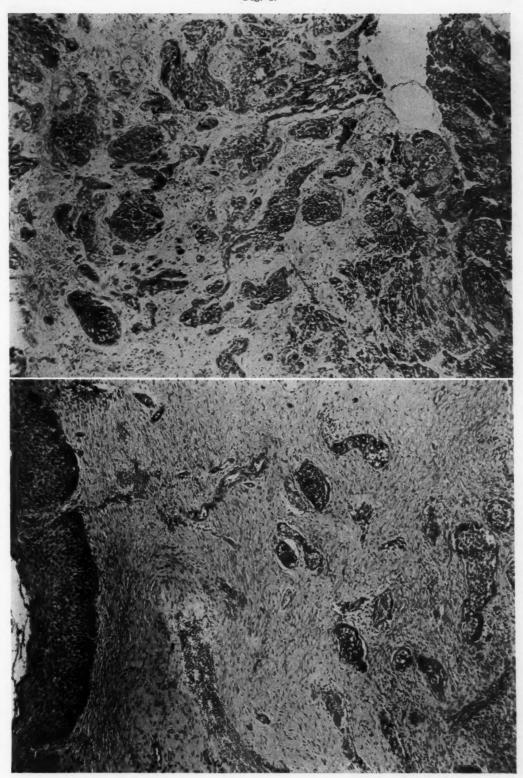


Fig. 2.

Fig. 1.—Invasive squamous-cell cancer of the vagina. Fig. 2.—Invasive squamous-cell cancer of the vagina.

These 2 patients were included in the 151 patients reported in 1952.¹ They are not included in the 275 patients reported in this paper. These are the only patients with Stage 0 cancer since these studies began who, to date, have shown invasive squamous-cell cancer of any of the pelvic structures. Whether the vaginal squamous-cell cancer in these two patients might represent "seeding" of the vaginal mucosa from the intraepithelial cancer of the cervix, or direct extension of the process, is problematical. It is also problematical that these invasive squamous-cell cancers started in multiple independent foci of abnormal cells.

The importance of follow-up on all patients, whether they are being followed in a conservative manner, or whether they are being followed after definitive treatment, is emphasized by these 2 patients. For all patients who continue to show neoplastic cells in cytologic smears after any type of hysterectomy, we have adopted the policy of removal of the entire upper vaginal mucosa, by partial colpectomy, in order that Stage 0 or early invasive cancer may be searched for and diagnosed. The procedure of removal of the upper vaginal mucosa is not difficult. There is little, if any, distortion of the upper vagina if adequate hemostasis is assured and if, in postoperative care, the upper vagina is kept patent by the daily use of vaginal dilators. Formation of epithelium is rapid in the areas of vaginal epithelial denudation. Shortening of the vagina has not been a problem.

Summary

A report is given of 275 patients with intraepithelial (Stage 0) squamouscell cancer of the cervix or cervical stump, who have had diagnosis and treatment in our clinic during the past eight and one-half years.

An attempt is made, by the use of descriptive tables, to place Stage 0 cancer in its proper perspective in the entire problem of malignancies of the female generative tract, as these malignancies are seen by our group.

From this small series, we can draw no valid conclusions. This series is simply the basis for consideration of an attempt to formulate how properly to manage the problem of Stage 0 cancer.

A review of the clinical material, as shown in the various tables, adds little noteworthy data to those of the 1952 report. Although the figures are not of statistical value, Table I shows that the incidence of intraepithelial cancer in the gynecologic patients was 0.58 per cent and in the obstetric patients the incidence was 0.57 per cent.

No significant alterations are found for age (Tables III and IV), for race and economic status, for marital status, or parity (Tables V, VI, and VII).

Table VIII shows clearly that Stage 0 cancers were found in cervices and in cervical stumps in which no clinical manifestations of disease were apparent to the examiners. If evidences of disease were present, they were in no way pathognomonic of Stage 0 cancer.

A comparison of treatment Tables IX, X, and XI in the original report of 1952 with treatment Tables X and XI in this present report shows among the clinicians of our department a definite trend to vaginal hysterectomy with conservation of the ovaries in our younger age groups. The majority feels that vaginal hysterectomy with removal of an adequate vaginal cuff is the operation of choice. It should be noted in Table X that of 237

gynecologic patients with intraepithelial cancer of the cervix, 57 are being followed with no further definitive treatments than multiple punch biopsies for 7 patients and cold-knife cone biopsies for 50 patients.

Discrepancies between the total figures for certain categories in the treatment Table X in this report and those in the treatment Tables IX and X in the original 1952 report are due to elimination from this series of a number of patients treated and followed elsewhere (uncontrolled and lost).

Table XI shows that of 38 obstetric patients with intraepithelial cancer of the cervix, 10 have received no more definitive treatments than multiple punch biopsies and 11 no more definitive treatments than cold-knife conizations.

The figures in Tables X and XI state a calculated risk we have assumed in following these patients who have not had definitive treatment.

Another expression of this assumed risk is found in Table XII which shows that 7 gynecologic patients with Stage 0 cancer of the cervix were permitted to become pregnant one or more times before definitive treatments were given. It is important to note that only one of these 7 patients has continued to show genital smear atypicalities. This patient had multiple biopsies only and not cervical conization.

Table XIII gives the data on the 11 patients, in a total of 38 obstetric patients who had Stage 0 cancer, who became pregnant after the diagnosis was established. Of these 11 patients, but 3 at the present time had had definitive operative treatment. Eight patients are being followed.

One obese, hypertensive patient died following vaginal hysterectomy.

No other significant complications occurred as a result of operations for diagnosis or treatment of Stage 0 cancer. Resuturing of the cervix for hemostasis was done in several patients who continued to bleed following cold-knife conization. Routine soundings control the problem of cervical stenosis.

One patient, of the 275 patients, had a depressive psychosis prior to diagnosis and definitive therapy and committed suicide despite psychiatric care. It is not felt that the diagnosis and treatment hastened her action.

No patient in this series has developed drug addiction.

In the discussion, an effort is made to show some of the problems of Stage 0 cancer as they involve many of the specialists of hospital technical practice as well as those of our own service.

A short summary is given of the clinical records of two patients in whom invasive squamous-cell cancer of the vagina was demonstrated years after definitive diagnosis and hysterectomy for intraepithelial cancer of the cervix. These two patients are subjects for many varied speculations.

To our knowledge none of the patients who are being followed without definitive treatment has developed invasive squamous-cell cancer of the cervix.

The follow-up is an important feature in the study of Stage 0 cancer of the cervix or of the cervical stump. It is essential that all patients whether they have had conservative or definitive treatment be followed with adequate

diagnostic techniques. Heavy obligations are assumed by anyone who elects to treat the lesion whether by conservative or definitive therapeutic methods. The "pooling" of data from many clinics must be expedited in order to clarify the confusion which now exists in criteria both for diagnosis and for the methods of treatment.

Data are presented on the number of follow-up visits and the duration of the follow-up periods for 60 of 75 patients who have Stage 0 cancer and who have had but multiple punch biopsies and cold-knife cervical conizations. The number of follow-up visits per patient ranges from 1 to 14, totaling 289 for the 60 patients. The duration of the follow-up periods ranged from 2 months to 6 years.

No patient in this series who has had definitive treatment for Stage 0 cancer of the cervix continues to show atypicalities in genital smears. Three gynecologic and 2 obstetric patients who had multiple punch biopsies or cold-knife cervical conizations of the cervix have persistent cytologic atypiae. The two obstetric patients have recently delivered and 2 of the gynecologic patients desire further pregnancies. The third gynecologic patient is 74 years of age and has severe cardiac disease.

It is important that two groups of patients in this series be followed closely for academic as well as for clinical reasons. The first group is comprised of those patients who had microscopic foci of invasion found in tissue specimens subjected to multiple block sectioning. There were 7 of these patients, 6 gynecologic and one obstetric. To date, none of these patients has clinical evidence of invasive cancer.

The second group is comprised of those patients who have not yet had definitive treatment. Patient 4 in Table XII is an outstanding example in this category. Faithful in follow-ups and with understanding, she refuses further diagnostic or treatment procedures. The diagnostic multiple punch biopsies were made just four years ago. The patient remains adamant in her intention to have another child. Periodic infertility on the husband's part has increased the difficulty of the situation.

Reference

 Carter, Bayard, Cuyler, K., Thomas, W. L., Creadick, Robert, and Alter, Robert: AM. J. OBST. & GYNEC. 64: 844, 1952.

Discussion

DR. JOE V. MEIGS, Boston, Mass.—In 1952, at the meeting of the American Gynecological Society in this same theater, I had the privilege of discussing the first of the papers on cancer in situ presented by Dr. Carter and his group of associates. Four of the original five authors have contributed to this paper and four other investigators have been added. Dr. Carter has obviously stimulated his entire staff to be on the alert and to participate in his very important study of the lesion known as carcinoma in situ.

I have reread my own discussion of Dr. Carter's paper No. 1, and I see no reason to change it. Some of the points in that discussion I will not repeat.

It is interesting that in the clinic at Duke they have averaged 32.3 cases a year for 8.5 years and in the last 3½ years the incidence has been 35.4 per year or approximately

the same. Therefore, the type of patient, the diagnostic ability of the staff, and the pathologists' diagnosis appear to be very consistent.

Recently Dr. Walter Dannreuther stated to me that the diagnosis of cancer in situ was very uncommon in his old department and now in his private practice. Why is this? I am sure it is not paucity of knowledge, but because of a lack of conformity in the diagnostic criteria of this lesion.

The most striking report I know of on this problem was presented in Boston in November, 1954, before the Inter-Society Cytology Council by Dr. Edward Siegler of Cleveland. He sent the histologic slides of 20 different cervical lesions to 24 different pathologists. The analysis of their diagnoses showed absolutely no consistency. Pathologists in the same department, the chief and his assitant, did not agree. This inconsistency is a very important one and may explain Dr. Carter's 35 cases per year and Dr. Dannreuther's very few.

One of the most important of Dr. Carter's observations is that although all of his department personnel are looking carefully for in situ cancer, only 11.3 per cent of the patients with the lesion were even considered as having a malignant lesion. Those who believe that it is safe to wait until the diagnosis of cervical cancer can be made with the naked eye must realize that they would miss nearly 90 per cent of the in situ cases.

The finding of practically the same percentage, 0.58 and 0.57, in both the obstetric and gynecologic patients emphasizes the importance of looking for the lesion and of confirming its presence in all age groups whether the patient is pregnant or not. My mathematics show that the Duke clinic has 27 patients with cancer in situ per year out of 4,786 gynecologic patients, or 0.56 per cent, and 4.4 patients, or 0.57 per cent, out of 764 obstetric patients.

The importance of removing enough vaginal cuff is obvious. We believe that before surgery is undertaken the vagina as well as the cervix should be stained with iodine solution and any unstained areas biopsied before definitive treatment. If this staining is done only at the time of operation, unstained areas of the vagina should be removed along with the uterus. The type of operation, abdominal or vaginal, is not important, but removal of sufficient vaginal cuff is. Conservation of ovaries in my opinion is most important, but this is a problem for discussion at another time.

We in our clinic have found that it is essential to follow all patients after treatment for any cancer of the cervix with vaginal smears. These should be taken on every visit to the clinic. By this means we have picked up numerous recurrences after treatment of in situ cancer as well as after surgery or radiation for invasive cancer.

One last plea is that all of us cease to allow patients to go without treatment after a diagnosis of cancer in situ has been made. There is plenty of evidence already that a large percentage of such lesions progress to invasive cancer. Some patients have been lost through this sort of investigation. I think it is careless, thoughtless, and very reprehensible to follow such a procedure. I believe that this is a very serious lesion and I protest against such callousness.

DR. ROBERT L. FAULKNER, Cleveland, Ohio.—In this series of patients, frequency and age incidence are about as in our own experience and correspond closely with most of the published reports. We have been interested in parity in connection with these epithelial changes and started some time ago to record the age at the first pregnancy thinking that perhaps such information might contribute something to the incidence of altered epithelium found in young women. The authors, however, as do others, have an appreciable number of nulliparous women in whom this disease has been picked up.

One of the troubles in handling the patient with Stage 0 carcinoma is that so frequently she has nothing the matter with her so far as she knows and the cervix looks normal. It is to be noted that in this series more than 88 per cent of the cervices were judged normal on pelvic examination. Without symptoms and with negative findings, there is the making of a fine psychological situation unless handled advoitly. One can easily understand that advice for an extensive operation based entirely on laboratory tests,

which the patient does not understand, must resemble chicanery or at least witchraft to many of them. Especially may psychological problems arise in connection with doubtful cases requiring close follow-up and repeat biopsies until a diagnosis is established. All the problems are multiplied if the state of pregnancy exists.

In this paper two groups of patients are reported upon that are of interest and mildly surprising. In the first place none of the 12 patients with subsequent pregnancies have gone on to invasive carcinoma. Other observers of these changes in pregnancy have not been so fortunate. Second, there have been no recurrences in 57 patients who were treated by biopsy only in 7 instances and by conization in 50. This is evidence in favor of a lesser treatment of this disease than is generally in vogue. It is desirable that the authors assure us that follow-up of these groups has been sufficiently long for them to be certain of their ground. It is to be hoped that some time a lesser treatment than hysterectomy may materialize as the standard in dealing with these epithelial changes.

Your discusser must confess that he does not at present enthusiastically share in the promotion of vaginal hysterectomy as the routine, or almost routine, treatment of this disease. This surgical approach traumatizes the cervix too much to be ideal in the handling of a carcinoma. In some instances the developed vaginal cuff may be turned down over the cervix for protection, somewhat as in the Schauta operation, but this is not feasible especially in many older women. Generally, unless the vaginal operation is to be an easy one due to associated genital relaxation and if one is to maintain a respect for the surgical specimen containing carcinoma, the conventional approach seems better.

DR. N. LOUROS, Athens, Greece.—I would like to emphasize one point, mainly because it has not been mentioned, namely, the difficulty of determining the exact location of the lesion which is helped by the colposcope. After having first taken smears routinely, we apply the Schiller test as a method of detection and then try to locate the lesion with the colposcope. We have found that the site of the lesion as visualized with the colposcope is at times quite different from the one indicated by the Schiller test and ordinary visual inspection. We believe that some diagnostic errors may be avoided by the use of the colposcope.

DR. CARTER (Closing).—This lesion does present many variables to confuse the clinician. This was brought out by Dr. Meigs in his remarks concerning Dr. Siegler's experience with his group of pathologists. We agree fully that there is a tremendous amount of variation in the criteria for the diagnosis of this lesion.

We also feel that the only way to diagnose the lesion is by constant emphasis on its possibilities, by applying cytologic techniques to each patient, and by having histopathologic confirmation.

The follow-up on these patients is discussed briefly in the manuscript and it will be seen from reading the paper the amount of work and the great number of visits required in any attempt to follow the patients.

We would emphasize the point that when preinvasive or invasive cancers are suggested by cytologic studies of patients who have had the uterus removed partial colpectomy is the method of choice for obtaining tissues for the pathologist. The operation is simple; epithelization is rapid; patency of the upper vagina is readily maintained by prosthetic exercises. We feel, in one of the patients described in the paper, that we were remiss in not doing a partial colpectomy for diagnosis at an early date.

We do use colposcopes and feel that they are of great value in focusing the attention of the doctors and the medical students on the cervix and the upper vagina. We did use the iodine test but we have more confidence in our cytology. We also feel that much must depend upon the doctor's ability to have the right to admit these patients to the hospital for proper cone biopsy without trauma to the epithelium of the portio or of the endocervix, or for proper partial colpectomy. We do not feel that the techniques of vaginal hysterectomy destroy the epithelium and certainly they permit removal of a very adequate vaginal cuff.

A STATISTICAL STUDY OF TWELVE POSSIBLE FACTORS GOVERNING POSTPARTUM BLEEDING IN THE FIRST SIX WEEKS*

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THE standard textbooks of obstetrics, such as that of Stander,¹ state that the lochial discharge normally becomes white or yellow between the tenth and fourteenth days post partum. This has not been my experience and yet patients ask questions about this point daily. Patients in my series seem to have made a normal recovery at the examination six weeks post partum in spite of deviations from this schedule and as a rule without special treatment.

The mechanism of involution of the placental site was well explained by the studies of Williams published in 1932.^{2, 3} He pointed out the initial hemostatic effect of uterine muscle contraction followed by the formation of thrombi at a slightly later stage. The prompt involution of the general endometrial cavity was noted and the slower involution of the placental site. The mechanism of exfoliation rather than granulation and scar tissue formation was clearly demonstrated and its great utility in the production of a scar-free endometrial cavity plainly shown.

In order to discover what produces these variations in amount and duration of bleeding during the first six weeks post partum, I have studied 389 private cases in relation to twelve possible factors listed below. As nearly as possible the cases were consecutive. Failure of the patients to report forced the deletion of some additional cases but an attempt was made to sample impartially and only from patients whom I delivered to minimize variations of observation and technique.

Correlation of the duration of bleeding with nine of the factors was studied by means of the coefficient of correlation "r" suggested by Pearson. This was easily accomplished because the observations in question could be easily expressed numerically and paired for the construction of the usual correlation table. The product moment formula used for the computation in question

was
$$r=\frac{\frac{\sum x'y'}{N}-C_xC_y}{\sigma_x\,\sigma_y}$$
. Complete correlation could produce a value of 1.0. The probable error of the coefficient of correlation "r" was obtained by

The probable error of the coefficient of correlation "r" was obtained by the formula $PE_r = \frac{.6745 \times (1-r^2)}{\sqrt{N}}$. It will be recalled that "r" would

not be considered as indicative of a correlation better than "o" unless it is at least 4 times its PE.6

^{*}Presented at the Sixty-sixth Annual Meeting of the American Association of Obstetricians and Gynecologists, Hot Springs, Va., Sept. 8 to 10, 1955.

The second method of computation was required when the categories were coarse. The amount of bleeding observed by the patient compared with the amount of bleeding during the menstrual period serves as an example. The amount observed by the patient could not be easily expressed numerically but the information could be grouped in categories such as heavy, moderate, and light. This type of relationship was expressed by C, the coefficient of mean

square contingency. The formula used for its computation was $C=\sqrt{\frac{S-N}{S}}.$

If no correlation exists C should equal .00. If correlation were perfect the value should be 1.00. Actually Yule⁵ has shown that in classifications as coarse as those studied in the present problem the maximum value could not exceed .816.

The patients were questioned at the six weeks' postpartum examination to find the number of days after delivery blood could be seen in the discharge and the amount estimated as light, moderate, or heavy. Where doubt was expressed amounts were compared with the amount lost by the patient each day of a normal period. The blood loss at delivery was measured by catching the blood in a hand basin pressed against the buttocks of the patient and the volume measured in a graduate. Losses on sponges and drapes were estimated and added to these figures later. Placentas were traced at once on paper for later measurement with a planimeter.

The twelve factors with a brief discussion follow.

- 1. Area of Placenta: Duration of Flow in Days.—It was thought that a large area might require a longer period of time for exfoliation and possibly the amount of bleeding noted externally might be in relation to the size of the surface from which it originated.
- 2. Birth Weight of the Infant: Duration of Flow in Days.—Since blood loss at delivery has been thought to have some relation to overdistention of the uterus it seemed possible that this might be projected even further to include involution of the placental site, possibly because of the influence of inferior contractility of the uterus with inferior original hemostasis at the placental site.
- 3. Length of Labor: Duration of Flow in Days.—Contractility was questioned as in Factor two. In a measure, the length of labor must be related to the efficiency of the uterine muscle as a contractile organ.
- 4. Blood Loss at Delivery: Duration of Flow in Days.—An attempt was made to test the relationship between initial hemostasis and later inefficient hemostasis. It was thought that original failures of the placental site might produce a persistently inefficient pattern not for hours but possibly for weeks after the initial separation of the placenta.
- 5. Elevation of Temperature (Duration): Duration of Flow in Days.—It seemed possible that the activity of bacteria might produce destructive changes in the thrombosed vessels of the placental site. This could be responsible for an extended length of the bleeding time or an increase in its amount. This thought was fostered by the pathological reports furnished from curettings

obtained from occasional patients who bled excessively during the postpartum period. Under this circumstance it has been my policy to palpate the placental site and to obtain material from it for study by gentle curettage. Marked evidence of infection is invariable in this material and a few specimens have shown no placental tissue. Elevations of temperature may not arise from disease in the placental site. Proof is sometimes hard to produce because antibiotic drugs were used promptly and in full dosage before clinical evidence was extensive. The uterus was not cultured. Temperatures as low as 99° F. were considered as abnormal in order that even very slight infections would be included in the study.

- 6. Elevation of Temperature (Duration): Amount of Flow.—This relationship was studied to check the possibility that patients might bleed more heavily in the face of infection even though the duration might not show change.
- 7. Maternal Hemoglobin: Duration of Flow.—Anemia has been accused repeatedly of producing poor involution and increasing the susceptibility to infection. It was included in the present study to see if it might have some relation to bleeding in the six-week period also.
- 8. Maternal Age: Duration of Flow.—The age of the patient was considered with the thought that the older patients, possibly due to vascular changes or changes in the ability of the uterus to contract efficiently, might demonstrate some change of pattern.
- 9. Parity: Duration of Flow.—This factor was considered as a possible influence upon the efficiency of the uterus because of repeated trauma. Some evidence seems to have been produced in the past that repeated pregnancy may influence the incidence of complications of delivery. It was thought that involution might also be disturbed even though the studies of Williams would indicate that scars do not result from involution of the placental site.
 - 10. Length of Menstrual Cycle: Duration of Flow.
 - 11. Length of Menstrual Period: Duration of Flow.
 - 12. Amount of Menstrual Period: Amount of Flow Post Partum.

These last three factors seem properly to fall in a single category. They represent an attempt to characterize the menstrual pattern of the patient to see if behavior of this type parallels in any way the behavior post partum. During the menstrual cycle endocrine factors produce marked and constant changes in the endometrium which involve at the time of the period both hemostasis and regeneration, even though not so far reaching as those which occur post partum. It will be recognized at once that no account is taken of such things as the bleeding and clotting mechanism of the patient which might quite properly be peculiar to each individual. Gross relationship was sought first.

In Table I in which the coefficients of correlation are listed it will be seen that evidence of correlation is too small to be significant with the possible exception of the twelfth correlation.

TABLE I. SUMMARY OF DEGREE OF CORRELATION OF POSTPARTUM BLEEDING WITH TWELVE FACTORS STUDIED

	r	PE_r	C
Area of placenta: duration of flow	.07	.034	-
Birth weight: duration of flow	.06	.039	
Length of labor: duration of flow	.004	.034	
Blood loss (at delivery) : duration of flow	.11	.034	
Elevation of temperature (duration): duration of flow			.03
Elevation of temperature (duration): amount of flow			.11
Maternal hemoglobin: duration of flow	.006	.036	
Maternal age: duration of flow	.08	.034	
Parity of mother: duration of flow	.06	.034	
Length of menstrual cycle : duration of flow	.05	.034	
Length of menstrual period : duration of flow	.10	.034	
Amount of menstrual period : amount of flow			.64
Average duration of bleeding		28 days	

In series involving few categories the reader will remember again that C is not as reliable as r obtained from a series with better distribution of categories. However, the maximum possible value for C under the present conditions was .816 and a value of .64 was actually obtained for the twelfth factor. This would seem to indicate much greater relationship than with any of the other factors considered. The others are so small that the inclusion of more cases would not be of further value, and they may be cast out at once as of no further interest.

The relative lack of statistical relationship between fever and the bleeding pattern of the patient is interesting. Where very marked disturbance of the bleeding pattern was noted, curettage usually revealed evidence of placental tissue still present in the placental site. Evidence of inflammation was noted as in the more unusual instances mentioned where only infected decidual tissue and clots were found in the curettings of the placental site. Since curettage was done only in the event of urgent need to control hemorrhage, too few cases were studied to yield statistical evidence of value. These few cases suggest, however, that the retention of placental fragments was possibly the most common precipitating factor. This may be more fundamental than we know. Slight to moderate increases of bleeding time and quantity still not requiring curettage may be the result of minor retentions of fetal tissue finally successfully separated and eliminated spontaneously by the patient. It is possible that the efficient separation and elimination of all placental fragments at the time of delivery are actually fairly rare even though no gross evidence of retention can be detected by the examination of the placenta at delivery. This may be an explanation for variation of the pattern post partum.

Some relation does seem to exist between the amount of blood lost by the patient at her usual menstrual period and the postpartum loss. As previously mentioned, this would encourage further study of the point. Better methods of determination of amounts of loss would be helpful in order that more and finer groupings could be established for statistical analysis. Since so much must depend upon the observation and judgment of the patient it will be hard to accumulate a reliable series of any size.

Summary

An attempt has been made to correlate twelve factors with the duration and amount of bleeding experienced by 389 private patients in the first six weeks after delivery. The only positive result showing sufficient correlation to be encouraging was the value .64 for C when amount of bleeding at the menstrual period was correlated with amount of bleeding in the following six weeks after delivery. Further study may be indicated with consideration of the bleeding and clotting characteristics of the patient. Even more interesting, however, would be a painless, inexpensive way of removing a biopsy from the placental site in the slightly and moderately protracted cases to evaluate the involutional progress and the placental tissue content.

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Discussion

DR. HAROLD L. GAINEY, Kansas City, Mo.—The statistical methods used in this study have been reviewed and found valid.

The continuation of lochia rubra beyond the period of what is regarded as normal was recognized in many of our cases and because of its frequency recorded in our postpartum observations. No attempt was made to evaluate quantitatively the amount and only those cases in which therapy was indicated as a result of excessive bleeding will be reviewed.

Factors considered most likely to be causative were retained secundines, and alteration in involution of the placental site and of the decidua vera. The observations of J. Whitridge Williams1 demonstrated the variability in the line of cleavage of the placenta and membranes and the amount of decidua which will be retained at the placental site or elsewhere in the uterus. He stated "that the amount of decidua retained may vary greatly in different specimens and all gradations may be observed varying from a thick layer on the one hand to minute decidual triangles between the serrated margin of the muscularis on the other." Dr. Schwegler stated, "Where very marked disturbance of the bleeding pattern was noted, curettage usually revealed evidence of placental tissue still present in the placental site. These few cases," he further states, "suggest that the retention of placental fragments was the most common precipitating factor."

This has not been our experience. A review of delayed postpartum bleeding in 5,250 patients disclosed that 23 patients required curettage. A summary of tissue reports showed the following:

Placental fragments, 5 cases.

Noninvolution of placental site, 8 cases.

Decidua and endometrium in varying phases of degeneration and physiologic activity both secretory and proliferative, 10 cases.

Of the 23 patients, menorrhagia was present in the history of one. All were multiparas, with previously normal records. In 8, with subsequent records available, there was no repetition of the experience.

It would seem that alterations in healing of the placental site and the decidua vera caused by undetermined factors are associated with multiparity more frequently than with primiparity. Occasional retention of placental fragments is responsible for excessive and prolonged bleeding following parturition.

The author stated, "Evidence of inflammation was noted as in the more unusual instances mentioned where only infected decidual tissue and clots were found in the currettings of the placental site." The criteria of infection used by the author interest me, as the extensive polymorphonuclear infiltration usually used by the pathologist may in these cases be only physiological as was demonstrated so well by Dr. William B. Hendry² with curettings from four areas in the uterus from 24 normal patients, 10 between the fourth and fifth days, and 14 between the ninth and eleventh days. Only one section showed chorionic villi. The most constant finding was extensive infiltration of polymorphonuclear leukocytes throughout the stroma of the degenerating decidua. All patients chosen for his study were afebrile.

This interesting statistical approach is none the less important by its negative results, as all of these questions must, at one time or another, pass through the minds of clinicians. It may be worthy of note and question, however, that of the twelve factors studied, the one resulting in significant results is the twelfth, the amount of menstrual period compared with the amount of flow post partum. The eleven others were associated with some definite numerical measure as maternal age, birth weight, duration of flow, etc. Is it possible that in the same patient, or patients, the evaluation of bleeding might be excessive for both menstruation and postpartum bleeding?

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DR. E. D. COLVIN, Atlanta, Ga.—I have been struggling with this paper for several weeks. I cannot understand the Pearson coefficient of correlation or the coefficient of mean square contingency, nor is it possible for me to understand how an evaluation of blood loss dependent on subjective estimation can be correlated with other factors and end up with figures preceded by a decimal point.

Dr. Schwegler chose an interesting and troublesome phase of clinical obstetrics for our consideration, and at the same time he asks an important question. Is there an etiological relationship between certain factors and the duration and amount of blood loss in the first six weeks following delivery? His results seem to indicate a positive correlation between the quantity of blood lost during the menstrual flow and the puerperium as the only one for the twelve factors considered.

There are, in my mind, two factors which he did not discuss, but which I believe are frequent and of great importance in the causation of prolonged and excessive blood loss during the first six weeks following delivery. I refer to (1) the factor of retrodisplacement of the puerperal uterus; and (2) the absence of breast feeding, elective or otherwise, on the part of the mother. Both factors evidently exert unfavorable influences upon myometrial function in the physiologic process of uterine hemostasis by altering the normal pattern of contraction during the puerperium.

In a review of the charts of patients delivered by the Bartholomew Obstetric Group, several series of 389 each, the same number presented by Dr. Schwegler, were studied for comparison. It was not possible to arrive at conclusions in respect to the volume of blood loss, and accordingly the duration of bleeding was considered. Cases in which bleeding was found due to retained fragments of placental tissue, as proved by spontaneous expulsion or operative removal, were excluded from the following groups.

In an unselected consecutive group of 389 recently delivered women, the average duration of postpartum bleeding was found to be four weeks. In a second group, in which the uterus was found in an anterior position, the duration of bleeding was found to be

between three and four weeks. In a third group where all were found to have a retroverted position of the uterus, the duration of bleeding was between five and six weeks. In other words, in the retroversion group the duration of bleeding was prolonged by two weeks. Frequently in this group the regular six weeks postpartum checkup had to be delayed because of prolonged bleeding.

In a comparison of the duration of postpartum bleeding among nursing and nonnursing mothers, it was found the average bleeding time for the nursing mothers was three weeks, but for the nonnursing mothers it was between five and six weeks, a difference of two to three weeks in favor of the nursing mother.

Our experience seems to imply that the factors of anterior position of the uterus, and reflex stimulation of the uterus through the medium of nipple stimulation are important in influencing favorably the duration of postpartum bleeding. The episodes of uterine cramps associated with breast feeding are common occurrences in the observations of the clinical obstetrician and usually portend satisfactory uterine involution and a shorter duration of postpartum bleeding.

In the presence of the more severe and persistent type of hemorrhage, we have found that a retained fragment of placental tissue, overlooked at the time of delivery, is the most frequent causative factor in this type of bleeding. As Dr. Schwegler has mentioned, the retention of small placental fragments, slowly separated and eliminated, may be an explanation for variation in the pattern of postpartum bleeding, but probably in a minority of cases, inasmuch as tissue obtained by curettage is usually found free of placental elements. Late recurrent puerperal bleeding, usually appearing five to six weeks after delivery, and more often among nonnursing mothers, has, in our experience, been associated with resumption of menstrual activity. It should not be confused with recent postpartum bleeding.

Although I cannot understand the statistical part of Dr. Schwegler's presentation, it is not my desire to deprecate his efforts. I congratulate him on his painstaking and time-consuming work and especially on his efforts aimed at an understanding of a very troublesome and annoying clinical problem which is so frequently encountered in the practice of obstetrics.

DR. SCHWEGLER (Closing).—I'm sorry to have created confusion by the use of statistical indices of relationship. I have distrusted clinical impressions for many years and have striven to find some objective measure to evaluate observed phenomena. It is wise, however, to bear in mind constantly the fact that statistical results are never more accurate than the original observations. Statistics are like meat grinders, you get good hamburger only if you put good meat in at the top side—the grinding thereof in no way influences the results.

CERVICITIS CLINIC-TWENTY-FIVE YEARS IN REVIEW*

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(From the Department of Obstetrics and Gynecology, Washington University School of Medicine)

In 1930 the late Dr. Otto Schwarz organized a cervicitis clinic for the referral of patients who needed a special study for classification of their benign cervical lesions. We undertook the study of cervicitis as to its etiology, occurrence, prognosis, and therapy. These studies were made available to the residents, assistant residents, nurses, and visiting doctors who were taking refresher courses in gynecology.

The personnel of the general Out-Patient Gynecological Clinic selected patients who had cervical lesions exclusive of acute gonorrhea and proved cervical cancer. These patients were to be treated by other specialized subclinics. It was the policy of the cervicitis clinic to avoid becoming involved with cases of vaginitis unless such cases were secondary to chronic cervical infection. A large number of such patients were referred to the cervicitis clinic, however. In the majority of such cases, there was marked improvement in the vaginitis when the cervicitis was adequately treated. Patients who had a primary vaginitis were sent back to the general gynecological clinic with recommendation for some specific therapy.

Relative Frequency of Cervicitis

In order to show the part played by the cervicitis clinic during the past twenty-five years, we graph the patient visits to the gynecological clinic in per thousand units, with the patient visits to the cervicitis clinic in per hundred units. In general there is an average relationship until the year 1947. From 1948 to 1955 the patient visits to the gynecological clinic rise in almost a straight line, while the patient visits to the cervicitis clinic fall in almost a straight line (Fig. 1).

Changing Therapy of Cervicitis

The five periods that make up the 25 year observations from 1930 to 1955 are shown in outline as the therapy and special work done in the cervicitis clinic. The first publication to come from the cervicitis clinic was "Treatment of Cervicitis by Cautery and Electrocoagulation" in 1931.

The first 5 year period, 1930 to 1935, showed the therapy to be mostly medical and surgical diathermy and antiseptics. Dr. Mortimer Hyams² was developing his technique of conization of the cervix and we were using his methods as well as experimenting with the use of electrocoagulation of the cervix. This latter procedure was carried out by the use of a small, curved knife blade as an active electrode to undermine the cervical lips and to destroy the endocervical canal. Our problem was to treat all benign lesions of the

^{*}Presented at the Sixty-sixth Annual Meeting of the American Association of Obstetricians and Gynecologists, Hot Springs, Va., Sept. 8 to 10, 1955.

cervix in ambulatory patients. At this time we felt that more tissue could be removed at one sitting without the risk of a primary hemorrhage by the use of this coagulation method.

The incidence of secondary hemorrhage and difficulty with the subsequent slough together with improvements in surgical diathermy equipment brought

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us later to the use of conizations as the first-choice procedure.

There was one other publication in 1932, "The Treatment of Pelvie Inflammation by Medical and Surgical Heat," by Dr. Grandison D. Royston and the author. A demonstration of cervical electrocoagulation in removing mass cervical tissue was presented by Dr. Royston to this Association at the time of the mid-year clinic meeting in St. Louis in 1932.

The 5 year period from 1935 to 1940 was an active and productive one. In 1936 we put into general use an anhydrous lactose sugar as a vaginal pack and as a home therapy for patients who inserted into the vagina large capsules containing the beta lactose. We had a colposcope for study of cervical lesions and changes produced by estrogens and conizations. We selected 40 patients

O.P.D. Patients Visits to Gynecological & Cervicitis Clinics

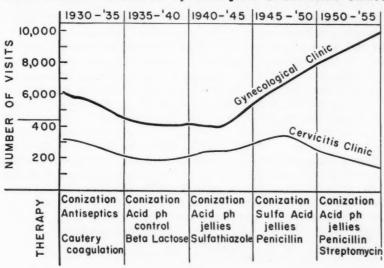


Fig. 1.

who had had a supravaginal hysterectomy and bilateral salpingo-oophorectomy to receive large doses of the newly released stilbestrol. The cervices of these patients underwent marked growth stimulation. An atrophic castrate cervix would return to its former pathological state. For example, many patients developed chronic cystic cervicitis. Others would show various degrees of papillary erosions. These changes were checked by both colposcope and biopsies. The endocervix would start secreting mucus and the vagina would become cornifield. It was noted that the degree of vaginal acidity would be increased if the high level of stilbestrol therapy was interrupted at regular intervals. This caused a shedding of the mature acid-fermentable vaginal cells and it occurred to us that perhaps this was physiologically significant. For, by the production of vaginal acid, the squamous epithelium of the cervix seemed to replace the columnar epithelium which had grown out from the endocervix as a result of estrogenic stimulation.

To check this theory we took patients who had benign cervical erosions and deep cervical lacerations which caused exposure of the endocervical canal and, by means of vaginal diaphragms, buffered acid jellies and buffered alkaline jellies were placed over the cervix. These patients reported to the clinic every third day for reapplication of the pH media. These experiments were carried out on regularly menstruating women. The same patients were subjected to a reversal of media for checked observations. In all cases the alkaline medium applied for 7 days or longer caused a softening of the squamous epithelium and a seeming proliferation of the columnar epithelium in replacing the squamous

epithelium.

In all cases where the acid medium was applied, the squamous epithelium became more prolific and the columnar epithelium seemed to be held in check at the normal level of the internal os. The cases of deep bilateral lacerations were particularly illustrative of these changes which were confirmed by multiple biopsies and colposcope examinations. The accumulative evidence supported our theory as to the etiology of cervicitis as being mostly related to hormonal changes affecting the pH of the vagina and portio of the cervix by contact. This led us to develop acid jellies which would be more efficient than the sugar

There were 4 publications in this 5 year period. In 1936, "Cervicitis—Five Years Experience With Diathermy." In 1937, "Vaginitis and Cervicitis." In 1938, "On the Etiology of Cervicitis," and also in 1938, "Cervicitis-Vaginitis Syndrome Therapy."

The period from 1940 to 1945 gave us sulfathiazole as an efficient and powerful means of stopping the gonococcus and streptococcus infections. With gonorrhea mostly eliminated as a cause of acute infection and with controlled acid vaginal pH, we now had effective methods of combating cervical erosions without resorting to the structural removal of eroded infected areas of the cervix. Conizations were continued, but the incidence of such operations was reduced.

In 1942 the late Dr. Dudley Smith, who was in charge of the gonorrhea clinic, suggested that we present to the American Congress on Obstetrics and Gynecelogy, which was meeting in St. Louis, our work on conization of the cervix and coagulation of Skene's ducts in selected smear-positive and culturepositive patients. These patients had not responded to oral sulfathiazole and he felt that the gonococcus was resistant to the drug because of the deeply buried nature of the infection. After wide conizations of the cervix and coagulation of Skene's ducts, the patients received vaginal packs of sulfathiazole and permanent cures were effected.

During this period there was a publication in 1943, "The Local Use of Acid Media and Sulfa Drugs in the Management of Cervicitis and Vaginitis."8

The next 5 year period, 1945 to 1950, showed the standardization of multiple sulfonamide jellies with acid pH control. This was also the time when penicillin and, later, streptomycin were put into use in the cervicitis clinic. Cases which were becoming sulfonamide resistant were now most effectively treated with

penicillin and penicillin-streptomycin therapy.

Vaginal cytology studies and cytology from cervical scrapings were stressed. Some effort was made to correlate these studies with the histological changes shown from multiple cervical biopsies. Unfortunately, we were unable during these years to come to any definite conclusions as to the value of cytology studies in classifying benign lesions of the cervix. The real value of cytology was for screening purposes in separating the frankly malignant cases from those that were not cancer. Biopsies were done for confirmation, however, in all cases of positive cytology, before referral to the cancer tumor clinic.

We became reluctant to use conization as a means of removing tissue for diagnosis for the reason that in questionable positive cases there was insufficient tissue left in the cervix for a biopsy study and the smears for cytology were affected by the inflammatory reaction from conization. For this reason patients with such questionable cervices were sent into the hospital for dilatation and curettage, and a wide endocervical and portio area was removed with a cold knife to avoid any possible heat distortion of removed tissue as might occur in the case of conization. Also subsequent cytology from cold-coned cases seemed to be more informative than after conizations.

The last 5 year period of the cervicitis clinic, 1950 to 1955, shows the absence of acute and subacute and chronic infections of the cervix. Patients are no longer permitted to have postabortal infections or postpartum infections. Also the incidence of laceration of the cervix at the time of childbirth is reduced. When such lacerations occur, the trend is definitely toward immediate

repair of the cervical laceration before repair of the episiotomy.

Cases of acute cervical gonorrhea are so rare that when one such patient did present herself to the clinic, the assistant resident and interns made a diagnosis of carcinoma. A biopsy was taken and only later did the correct diagnosis appear. In our general Out-Patient Department gynecological clinic, early cancer is seen 20 times more frequently than acute cervical gonorrhea is seen.

With gonorrheal, postabortal and postpartum streptococcus infections eliminated by antibiotics, we expect to see little or no cervicitis as a result of infection. This leaves us the benign concentric reversible erosions of the cervix, polyps, and the persistent forms of papillary erosions mostly of the eccentric

type. Also, there are still a few cases of chronic cystic cervicitis.

The etiology of these benign lesions is probably hormonal. The simple concentric erosions are for the most part reversible and do not require conization therapy. The persistent type of papillary erosions which bleed and are of the eccentric type are best treated by conization. Polyps are removed with base tissue, and the Nabothian cysts of the cervix are opened for drainage without the use of a cautery.

No patients are subjected to conization until the result of multiple cervical biopsies from the endocervix and portio is recorded. This we feel is of the essence not only to eliminate the possibility of an early cancer, but to classify the histological structure of the cervix before removing too much cervical tissue which might be of later value in studying epithelial hyperplasia with nuclear abnormalities, especially as to such cases as might be reversible.

Follow-Up Results for Certain Types of Therapy

We selected 69 patients with benign cervical lesions (Table I) for a special study to determine what happened to a cervix which had been coned and later removed with the uterus at the time of a complete hysterectomy for some uterine lesion, or cases in which a repeat biopsy showed a recurrent cervical lesion.

Twelve cases of chronic cervicitis came to complete hysterectomy some $5\frac{1}{2}$ years after conization of the cervix. The average age of these patients was 44 years and the average parity was one and one-half. Pathological report of the cervix at hysterectomy showed 2 cases of endometriosis, 8 cases of chronic

cervicitis, and 2 cases of papillary erosion.

There were 15 cases of papillary erosion. Five of these patients had a complete hysterectomy some 5 years later. The average age was 39 years and the average parity was three. In all 5 of these cases the pathological report was chronic cervicitis. Ten of these cases came to repeat biopsy. Eight showed chronic cervicitis and 2 showed a normal cervix.

There were 3 cases of leukoplakia. The average age was 48 years and the average parity was three. At the time of complete hysterectomy, some 1 to 4 years later, 2 showed papillary erosion and 1 case was chronic cervicitis. There was no return of leukoplakia.

TABLE I. BENIGN CERVICAL LESIONS SELECTED FOR SPECIAL CERVICITIS STUDY

PATHOLOGICAL REPORT AT TIME OF CONIZATION	AGE AND PARITY OF PATIENT	INTERVEN- ING YEARS		REPORT AT TIME OF RE-	COMMENTS
12 cases chronic cervicitis		2 to 10 Average 5½ years	8 chronic cervi-		Benign cervical changes noted
15 cases papil- lary erosions	Average 39	Average 5 years	5 chronic cervicitis	8 chronic cervi- citis 2 normal cervix	proved
3 cases leuko- plakia	45 to 51 Average 48 years Average para	years	2 papillary ero- sion 1 chronic cervi- citis		No return of leukoplakia
22 cases basal- cell hyper- plasia	30 to 50 Average 40 years Average para	Average 4 years		changes	No Ca. in situ so far 4 years average
13 cases epithe- lial changes	40 to 49 Average 45 years Average para	Average 2 years	citis	10 benign squa- mous meta- plasia	so far
	40 to 50 Average 45 years Average para		Chronic cervicitis Epidermization		Little change
1 case normal cervix	41 years para		Adenomyosis Chronic cervi- citis		Endocrine effect

69 Benign Lesions

22 Cancer

91 Total Special Observation

Of 22 patients with basal-cell hyperplasia who had had conization, 2 came to complete hysterectomy and the pathological report was chronic cervicitis. The 20 remaining cases showed epithelial changes of benign squamous metaplasia at the time of repeat biopsy. No cases of carcinoma in situ were discovered in the 4 year average interval from conization to the latest pathological report of biopsy tissue. The average age of these patients was 40 years and the average parity was two.

There were 13 cases of epithelial changes reported at the time of conization. The average age of these patients was 45 years and the average parity was two. Three of these patients came to complete hysterectomy. Two cases showed chronic cervicitis and 1 case showed epidermization. Ten patients who had repeat biopsy studies showed squamous metaplasia. There were no cases of carcinoma in situ reported in this group after an interval of 2 years between conization and subsequent biopsy of cervix tissue.

There were 3 cases of Nabothian cystic cervicitis at the time of conization and some $1\frac{1}{2}$ years later, at complete hysterectomy, the cervix showed chronic cervicitis with epidermization. The average age of this group was 45 years and the parity three.

There was one case of a normal cervix at the time of conization and 5 years later this patient came to complete hysterectomy and the pathological report

was chronic cervicitis with adenomyosis.

The 69 cases of benign cervical lesions in which conization was done, and in which subsequent pathological reports of the cervix recorded a wide variety of benign lesions still existing or having developed, indicate that conical removal of cervical tissue does not prevent changes in the remaining cervical tissue. It is true that all these cases were associated with benign uterine changes such as myoma, endometriosis, chronic subinvolution, or uterine prolapse. We believe that under estrogenic stimulation these cervical lesions developed. It is quite misleading to judge the effectiveness of the conization by the gross appearance of the portio of the cervix. Most of these 69 cases exhibited little evidence of the changes shown to be present by microscopic examinations of the endocervical tissue.

Cancer of Cervix in a Cervicitis Clinic

It is the contention of some authors (Table II) that conizations and correction of benign lesions reduce or eliminate the chance of cancer in the cervix. We were interested in this aspect of the work done by us in the past 25 years. Dr. Sudholt checked the gynecological cervix cancer clinic to see if any of these patients might have had conizations in our clinic. He found only cases where cancer was detected at the time of conization, but no cases were discovered where cancer later developed in a coned cervix from our cervicitis clinic. It would have been very easy to draw the erroneous conclusion that our cervicitis clinic had contributed a real cancer prevention. We remembered that no known cases of cervical cancer were referred to the cervicitis clinic. Also, we performed no conizations on patients without a repeat multiple biopsy. Yet 10 cases of early Type I carcinoma were discovered at the time of conization, and 5 cases of carcinoma in situ were picked up at the time of conization. In the other patients who were proved not to have cancer at the time of conization, it would, indeed, be unusual if such patients later developed cervix cancer, shall we say, in spite of conization.

TABLE II. PATIENTS WITH CERVIX CANCER SHOWN AT THE TIME OF, OR DEVELOPED AFTER, CONIZATION

NO.	PATHOLOG- ICAL REPORT AT TIME OF CONIZATION	AGE AVERAGE	PARITY AVERAGE	INTERVEN- ING TIME FOR CA. TO DEVELOP	PATHOLOG- ICAL REPORT AT TIME OF REPEAT BIOPSY	I ICAL REPORT	COMMENTS
10	Carcinoma, Type I, early in- vasive	26 45 40	ii v iv		Type I to II 1 case ?Ca.	ably in situ	Biopsies showed no. Ca. be- fore coniza- tion
5	Carcinoma in situ	$\frac{30}{42}$ $\frac{40}{40}$	i iv iii	0 to 3 years Average 1 year		4 cases Ca. in situ 1 case chronic cervicitis	All patients alive and clear
5	Chronic cervicitis	29 47 43	i v iv	6 to 8 years Average 7 years	Invasive Ca Type III and 1 Type IV		X-ray and ra- dium ther- apy, all alive 1 terminal
2	Normal cervix	30 52	i iii	3 years 7 years	Type II Ca		x-ray and ra- dium ther- apy, 1 alive and 1 with positive glands

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Two patients in my private practice had cervical cancer, one 3 years and one 7 years after conization, with a pathological report of normal cervix at the time of conization. There were 5 patients in our cervicitis clinic who had had conical excisions or conizations elsewhere for benign lesions and we detected invasive cancer present in the remaining cervical tissue some 6 to 8 years later.

We seriously considered ways and means of contacting every patient treated in the cervicitis clinic in the past 25 years, but we were told that we could not expect to reach more than 25 per cent of these former patients. In other words we were uninformed as to the follow-up on 75 per cent of our clinic patients.

Now again referring to the 22 patients with cervix cancer shown at the time of, or developed after, conization, biopsies showed no cancer before conization, yet after conization and at hysterectomy 5 cases showed carcinoma in situ and one case showed chronic cervicitis. These patients' ages were from 26 to 45 years and averaged a parity of three.

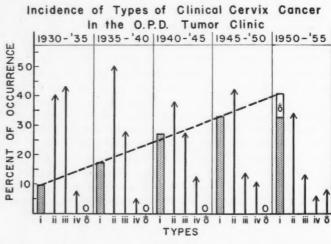


Fig. 2.

The 16 remaining cases showed cancer at the time of a repeat biopsy even after conization. Their ages were from 26 to 47 years and average parity was four. Thus conization did not prevent cancer in 7 cases, or completely remove cancer in the remaining 15 cases with one exception, where a case of carcinoma in situ three years later showed only chronic cervicitis at hysterectomy.

In order to arrive at the occurrence figures of cervical cancer in our tumor clinic for the past 25 years, Dr. Sherman divided the cases as to the clinical classifications Types I, II, III, IV, and $\overline{0}$ cancer, carcinoma in situ (Fig. 2). He showed that from 1930 to 1955 the detection of Type I cancer has gone up in a straight-line graph from 10 per cent to 18 per cent to 28 per cent and begins to level off at 33 per cent in the years 1945 to 1950. It remains at 35 per cent for the years 1950 to 1955. If, however, we add the per cent of detection of carcinoma in situ cases to the detection of Type I cases, we would have a continuation of a straight line graph with a 41 per cent detection.

More cancer is being detected in the very early stages, thanks to patient-doctor education. Wheeler and Hertig¹⁰ report similar figures from their clinics and their review of the literature as to the occurrence of early cancer associated with benign cervical lesions.

Comments

With the control of syphilis, gonorrhea, postabortal and postpartum infection, the number of cervices damaged by infection is reduced to a minimum.

With the general practice of better obstetrics and the immediate repair of cervical lacerations at the time of delivery, the number of cases of cervical lacerations and resulting ectropion are reduced to a minimum.

With the better understanding of the hormonal nature of simple concentric cervical erosions, and the reversible trend with the acid pH medium contact, there are fewer conizations and cauterizations (thermal or chemical) practiced (Fig. 3).

With better methods of cancer detection, cytology, multiple biopsies from the endocervix and portio, and cold conical excisions at the time of dilatation and curettage, conizations for diagnostic purposes have been reduced to a minimum.



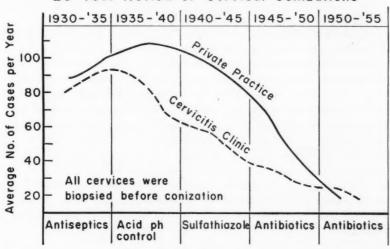


Fig. 3.

At this stage of our report we may well ask, of what future use is a cervicitis clinic? Conizations are still used for proved papillary erosions of the cervix, especially of the eccentric type which are prone to bleed. Benign cervical lesions must still be observed and cervical polyps removed. But most important is the continued observation of all cervices with simple epithelial hyperplasia with nuclear abnormalities, noninvasive and borderline cases with doubtful frank invasion of the cervical glands.

Conclusions

Perhaps it can be shown what histological changes are most often associated with carcinoma and whether such changes are in the role of an etiological factor or present by association with some common carcinogenic agent.

It does *not* seem to us that the elimination of infection and structural removal of benign lesions has in any material way lessened the incidence of carcinoma in situ and Type I invasive cervical cancer.

Conization does not necessarily eliminate the recurrence of benign or malignant disease of the cervix in spite of the normal appearance of the cervical portio.

The general use of antibiotics has removed the cervical infections, postabortal, postpartum, and venereal types, thus greatly reducing the need for coniza-

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Discussion

DR. MORTIMER N. HYAMS, New York, N. Y .- Since the time of Strogonoff, who first described chronic infection of the cervix as a distinct clinical entity, much has been accomplished. Innumerable methods of treatment have been advocated for its relief, from simple local applications to radical surgical procedures, even total hysterectomy. With the establishment of such clinics as described by Dr. Roblee and the work of others, there developed a better understanding of the various factors associated with chronic cervicitis.

Preventive medicine plays a most important part in gynecology and obstetrics, especially so with chronic infection of the cervix. Here much has been accomplished by education of the physician to the early recognition of pathology of the cervix and the eradication of its cause, meticulous care with instrumentation and the prevention of trauma, better obstetrics with prenatal and postnatal care and examination of the cervix following delivery. With the advent of antibiotics a new phase in the control of cervical infection was established. The further discovery of the broad-spectrum group of antibiotics has increased the use of this type of therapy.

At our clinic, it is our custom not to depend on conization in preference to all other methods but to use that modality which in our judgment best suits the condition of the cervix. This is based on the age of the patient, the bacteriological findings, and the degree of disease present. Due consideration is given to complicating factors such as pelvic inflammation, uterine and ovarian tumors, parametritis, and those conditions producing pelvic congestion. Routine cytological as well as biopsy examinations are done on all patients. Macroscopic examination of the cervix to determine the degree of pathology is not adequate. Biopsy of the external os deep into the stroma of the cervix and taken from several areas will give more precise information about the status of the abnormal process.

There has been a decrease in the incidence of chronic cervicitis in the past years. This cannot be solely attributed to the use of the more modern methods of treatment. Lay education brought about by the publicity given to cancer control and the prevalence of group insurance, by which a thorough pelvic examination can be obtained, have all been very important factors in the early recognition and treatment of cervical pathology. Notwithstanding, far too many patients are still seen with chronic cervicitis. I am sure that Dr. Roblee did not mean to convey the idea that chronic cervicitis is rarely seen today.

There have been recurrences of chronic cervicitis following conization and after any other electrical modality used to destroy endocervical tissue. The possibility of reinfection following labor or other trauma cannot be overlooked. Depending upon the age of the patient and the extent of the inflammatory process, total hysterectomy is at times indicated.

DR. ROY W. MOHLER, Philadelphia, Pa.—During the period from 1930 to 1935 I began to use electrocoagulation of the cervix and endocervical resection with the endotherm as a method of treating cervical disease. We also evolved at this time a culture of viable Döderlein bacilli in a vehicle of beta lactose for the treatment of leukorrhea. Biopsy of the cervix, at that time, was not routine practice as it is now, and treatment of the cervix was instituted most frequently for the treatment of vaginal discharge, when the cervix was thought to be diseased.

Since this period of more than twenty years ago, the management of cervical disease has evolved into a campaign to teach physicians to understand better the anatomy, physiology, and pathology of the cervix so that we may be able to recognize early malignant changes

and perhaps, by treatment, prevent the progress of malignant disease.

I was particularly interested in the observations made of the 69 patients who had the cervix treated by endocervical resection and whose cervices at some later time became available for histological study. The results from this observation are what one would expect since there was no way of determining the extent of the disease at the time of the first procedure and no assurance that all of the diseased tissue was removed at that time. It is significant that no malignancy was discovered in any of this material. My own observations correspond and I believe the conclusion is justified that proper treatment of the diseased cervix will prevent the development of cancer in all but rare instances.

We need an acceptable standard for the evaluation of a normal cervix. My conviction is that all misplaced endocervical tissue should be destroyed so that the squamocolumnar junction occurs in an area where it would not be exposed to the acid vaginal secretion. Heteroplastic endocervical tissue is relatively fixed in its distribution. Progressive inflammatory changes may occur in it during the procreative period but if completely destroyed,

will not recur even after a normal labor.

The terminology, such as erosion, eversions, congenital eversions, papillary erosions, concentric erosions, and eccentric erosions, and other terms, seems to have no uniform connotations. I would suggest that this organization become active in a study of terminology and in some way provide from this study a standardization of nomenclature for gynecological diseases generally and for those of the cervix particularly.

DR. ROBLEE (Closing).—Dr. Hyams asks if chronic cervicitis still exists in a sufficient number of patients to warrant a separate cervicitis clinic. We are beginning to think that the answer is "no." We feel that the few cases can now be handled as a part of the general Out-Patient Gynecological Clinic and that a special clinic should be started for the classification and therapy of benign, borderline benign, and carcinoma in situ cervical lesions.

Dr. Mohler is convinced that we need a new terminology to describe epithelial changes which we now feel are not a result of chronic infection and should not be called cervicitis. With acute and chronic infections now under control we can and should get some uniformity into our descriptions. We can combine our observations when we talk about simple epithelial hyperplasia, epithelial hyperplasia with nuclear abnormalities, noninvasive and borderline cases with doubtful frank invasion.

The question has been asked if conization does not remove the benign lesions that are provocative of cervical cancer. The answer is probably "yes," but our new problem is to determine just what epithelial changes are precancerous. We know that cervical conization is inadequate as a permanent therapy for cancer in situ, but it is useful in delaying the process in young women, who may thus have the time for limited childbearing before elective hysterectomy.

MEASUREMENTS OF ALDOSTERONE IN THE ECLAMPTOGENIC TOXEMIAS OF PREGNANCY*†

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LTHOUGH the sodium-retaining propensity of the lipid fraction of the urine of certain patients had been recognized since 1950,1 the responsible hormone—aldosterone—was not crystallized until 1953,2 nor chemically identified until 1954 (Fig. 1).3,4 This steroid, found in beef adrenal glands and adrenal venous blood, has also been identified in the urine of patients with heart failure, 5 nephrosis, 6 cirrhosis of the liver, 7, 8 pre-eclampsia and eclampsia.9, 10, 11, 12

ALDOSTERONE

Fig. 1.—Chemical configuration for aldosterone. In solution the steroid is believed to exist in equilibrium between the two forms.

Aldosterone has the most vigorous sodium-retaining action of any of the steroids yet identified. Its potency in this respect is usually quoted as being 20 to 30 times as great as that of desoxycorticosterone, 13 although by some techniques of measurement it is cited as being from 85 to several hundred times as powerful a sodium retainer as DCA.14, 15 In the adrenalectomized dog its potency in maintaining life and electrolyte balance is 10 to 30 times that of DCA and 500 times that of hydrocortisone.16

^{*}The work reported here was aided by Grant No. 561M3 from the Cleveland Area Heart Society. The steroids employed for standardization of the chromatography were generously supplied by The Upjohn Cor.pany and the Schering Corporation.

†Presented at the Sixty-sixth Annual Meeting of the American Association of Obstetricians and Gynecologists, Hot Springs, Va., Sept. 8 to 10, 1955.

During the past two years at MacDonald House the measurements reported here have been carried out of the sodium-retaining activity of the urinary corticoids in toxemic women and the aldosterone excretion rates determined. In addition to reporting these measurements the present paper is concerned with exploring the physiologic mechanisms involved in the appearance of this hormone in the urine of women with the eclamptogenic toxemias.

Methodology

The techniques for measuring aldosterone have been repeatedly recorded in the literature of the recent years. The urine was chloroform extracted following the technique of Leutscher¹⁷; placental extracts were prepared by mincing the placenta and applying the extraction technique Farrell¹⁸ employed for adrenal venous blood. The animal assay has used the adrenalectomized rat,¹⁹ although the ether reflex was employed to empty the bladder before and after each "run" rather than tying the urethra. The sodium and potassium levels of the rat urine were determined by flame photometry, aldosterone causing a retention of Na and an increased excretion of K.

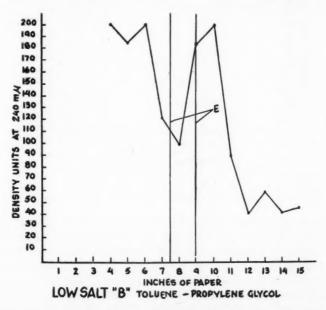


Fig. 2.—Distribution curve of the chloroform-soluble fraction of urine: first fractionation. Inches 4 through 15 are eluted for the second chromatography. The localization of the cortisone control spot is indicated by the vertical lines.

In such animal assay, the impact of aldosterone on the sodium excretion, or on the Na/K urinary ratio is impressive, but positive changes in the assay alone do not indicate the presence of this particular steroid. Actually this assay represents a technique for measuring the sodium-retaining activity of the chloroform-soluble constituents of the patient's urine, and when applied to similar patients (i.e., women in the last trimester of pregnancy) gives a comparative indication of the sodium-retaining factor (SRF) in the urinary corticoids.

The same chloroform-extracted residue which in ethnol-sesame oil solution is employed in the adrenalectomized animal assay, can, in chloroform

solution, be fractionated by paper chromatography.^{20, 21} Aldosterone moves to a spot behind cortisone¹⁸ in a propylene glycol (½ strength)—toluene system, but once again the mere finding of a spot in this area does not prove the presence of this particular steroid in active form.

The chromatographic studies reported here have consisted of an initial separation as previously indicated using E as the standard on 2-inch paper. The strips are then cut into 1-inch units which are eluted with methanol and read in a Beckman spectrophotometer under ultraviolet at a wavelength of 240 millimicrons. An example of the curve obtained on such a reading is indicated in Fig. 2.

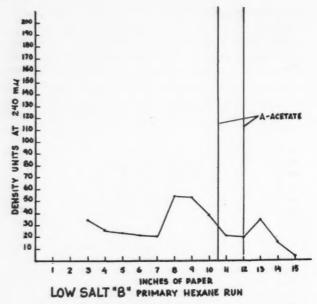


Fig. 3.—Refractionation of the peak eluted from the curve in Fig. 2. Control steroid A-Acetate localized as indicated.

The methanol solutions which represent the peak of this curve are then evaporated down to a residue which is dissolved in chloroform and rechromatographed in a propylene glycol (full strength)—hexane system using compound A acetate as the standard. Again the strip is cut into 1-inch lengths, eluted with methanol, and read as before (Fig. 3).

This second chromatography will show three peaks, and all of them are eluted again and rechromatographed on 1 inch paper with A acetate as the standard. At this point the peak behind the A peak (Fig. 4) is eluted with methanol, evaporated to a residue activated and taken up in an ethanol mixture for assay in the adrenalectomized rat. The area included under the peak of the curve quantitates the amount of steroid isolated, although the assay is required to indicate whether or not all of this material is active.

I. Sodium-Retaining Factor Assay in Toxemic Patients .-

A total of 63 assays of the sodium-retaining activity of the urinary corticoids were carried out in 51 patients. Seventeen of these patients were normally pregnant in the last trimester; 5 had displayed some early tendency to increase in blood pressure (average 130/90) with excessive weight gain, while one had a trace of urinary protein, one showed a 1 plus proteinuria, and the other 3 were protein free. Of the 29 patients with toxemia, 4 had eclampsia, 12 had severe and 13 mild pre-eclampsia.

Twenty-four hour urines were collected prior to the institution of any treatment other than bed rest (12 hours in those cases where the medical necessity forced earlier therapy), and a 300 c.c. aliquot extracted. The results of these initial assays, as recorded in Fig. 5, are expressed as the percentage of the control rats' sodium output which was excreted by the test rats, and are equilibrated to a 30 minute patient urinary output for the collection period. The sodium-potassium ratio of the test animals expressed as the percentage of the sodium-potassium ratio for the control animals were, in these studies, parallel to the sodium excretion expressed as a percentage of the excretion of the control rats, and the latter figure has been used throughout.

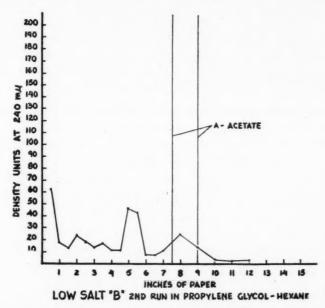


Fig. 4.—Final chromatographic curve. The peaks are eluted individually for bioassay.

A consideration of these results (Fig. 5) indicates that the group of women with toxemia demonstrate a marked increase in the SRF compared with the normal pregnant patient. The mean sodium retention of the assay animals for the toxemic group is 84 per cent and of the normals is 104 per cent. This confirms the observations of Chart and associates^{9, 10} and of Venning¹¹ as to the biologic activity of these steroids in women with pre-eclampsia.

Other observations are available from these data, however: (a) Many of the nontoxemia group demonstrate as much sodium-retaining activity as the mean for the toxemia group. These women displayed at most dependent ankle edema and had no other clinical findings suggestive of toxemia. (b) Similarly, several of the toxemia patients overlap well into the normal range. (c) Not only is there this individual overlapping between the toxemia-nontoxemia patients; but there is a negative correlation with the severity of the toxemia: the patients with mild toxemia showing more SRF than the eclamptic women. (d) The 5 "prodromal" patients—the women with mild "pre-toxemia" symptoms—showed no results that could be correlated with their clinical course. Four of them responded to ambulatory medical management; one progressed to mild pre-eclampsia; this one patient's assay had indicated no sodium-retaining activity in the urinary corticoids.

Additional studies were made on 5 patients who were undergoing diuresis.²² In 3 of these the preliminary studies had indicated a high degree of sodium-retaining activity. In none of them was there a significant degree of such activity during the period of diuresis. Two of these women were apparently responding to bed rest alone; the other 3 had received ammonium chloride. The disappearance time for SRF after delivery, which was followed in 3 patients, indicated no biologic activity after the third postpartum day. In 2 of these 3, however, the postpartum diuresis had clearly started by this time

A series of 5 placentas from toxemic patients failed to show a strong sodium-retaining fraction. All of these, however, were from patients who had been treated with some degree of success clinically prior to the delivery of the placenta. Furthermore, all placentas—whether the patient has had toxemia or not—yield a hexane-insoluble, choroform-soluble fraction which has some mild sodium-retaining propensity. Finally, on chromatography even the normal placenta produces a spot in the aldosterone area, although to date we have not assayed that area for its biologic activity.

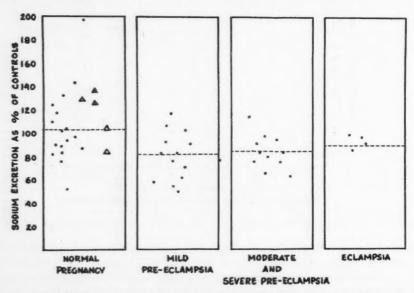


Fig. 5.—Results of SRF assay in 51 pregnant women. Each dot represents one 30 minute aliquot of urine, the assay results being reported as the per cent of the control rats' sodium excreted by the test rats. The \triangle figures in the Normal Pregnancy column indicate the "pretoxemia" patients. The horizontal lines represent the mean value for the group.

Comment

The eclamptogenic toxemias of pregnancy can apparently be grouped with other clinical entities which show edema and are associated with the fairly consistent appearance of the sodium-retaining factor in the urine (cirrhosis, nephrosis). Simply because this powerful sodium-retaining factor can be extracted with a fair degree of consistency from the urines of patients with clinical syndromes characterized by edema, however, it does not automatically follow that this substance is the cause of the edema. Not all of the women in this study, nor all patients reported in the literature who excreted significant amounts of aldosterone-like substances in the urine, have dem-

onstrated clinical edema^{22, 23, 24}; neither in this study nor in Venning's¹¹ are the amounts excreted proportionate to the severity of the clinical syndrome; the "prodromal" patients have not excreted it consistently, and the patient with diuresis loses it, although in other respects her clinical picture may remain as grave. Leutscher²⁵ has pointed out that many of the alterations observed in renal and endocrine function may be the result, rather than the cause, of the disease process. Furthermore, it is not yet proved that excretion means an increased production of this hormone.

In considering the mechanism of appearance of this substance in the urine of toxemic women, however, it is well to remember that aldosterone causes not only the sodium retention which is its most conspicuous effect, but that it also results in the elimination of potassium. Of these two actions the retention of sodium and the elimination of potassium—the latter is obviously of greater importance in human homeostasis. An elevation of blood potassium kills; indeed the principal function of the artificial kidney is to lower the potassium level rather than the level of nitrogenous waste products. Under these circumstances it is almost inconceivable that there should not be a protective mechanism which can be triggered to eliminate excess potassium.26 If such a mechanism had the coincidental tendency to retain sodium, or if the patient were particularly susceptible to sodium retention, the accumulation of salt and water might well be a by-product of the need to eliminate potassium. While such a hypothesis must remain, at the moment, largely conjectural, additional studies were undertaken to explore the possible mechanism by which aldosterone is mobilized in the pregnant patient.

II. Mechanism of Apperance of Aldosterone.—

A. Steroid administration: While on a general diet, a group of 6 women in the last trimester were given variously progesterone, estrogens, or cortisone, and their subsequent urine collected for SRF assay. These were acute experiments in which the steroid was administered during the daytime and the 12 hour urine collection carried out the following night. Sodium estrone sulfate was given in 40 mg. doses intravenously twice during the day; for the patients receiving progesterone the dosage was 200 mg. intravenously during the day²⁷; the cortisone patients received 50 mg. intramuscularly twice during the day preceding collection of the urine specimen for assay. As would be anticipated, the administration of these steroids which physiologically increase during pregnancy did not "trigger" an increase in SRF in the patients' urines.

B. ACTH administration: It has been reported that ACTH does not increase the aldosterone output. The experiments leading to this observation, however, were single-shot doses of ACTH in the nonpregnant subjects. A group of 5 patients normally pregnant in the last trimester were given 40 units of ACTH (1 c.c. Acthar Gel) daily for 5 days. Urine collections were made each night from 8:00 p.m. to 8:00 a.m. and assayed. Fig. 6 indicates the progressive changes in SRF in one of these. Three of the women in this portion of the study showed marked day-to-day variations which could not be clearly interpreted; 2, however, showed increased sodium-retaining activity at the end of the 5 day period of treatment. While no final conclusions can

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be drawn from this small group, we are not inclined at the moment completely to dismiss ACTH as contributing to the mechanism of the production of aldosteronelike steroids in pregnant patients.

C. Sodium restriction: Leutscher²⁹ has pointed out that a sharp restriction of sodium intake will markedly increase the aldosterone output in normal males. Five normal pregnant women in the last trimester were restricted from added table salt after the preparation of their food. The calculated estimations of their reported diets gave them the sodium chloride equivalent of 3 Gm. or less per day. Urine specimens were collected after a minimum of 7 days on this regimen, fractionated chromatographically, and the aldosterone peak assayed for activity. These women, after such relatively mild sodium restriction, were found to be excreting an average of 40 micrograms of aldosterone per day. The 8 control pregnant patients on ad libitum sodium intake produced 18 micrograms per 24 hours.

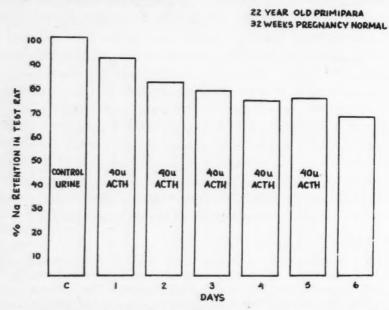


Fig. 6.—Daily assays on 30 minute aliquot of urine from pregnant patient on ACTH. No ACTH given sixth day. Height of bar indicates per cent of Na excreted by test animal in contrast to that by animal receiving extract of control urine.

These studies were made on pooled 72 or 96 hour specimens, and this fact, plus the smallness of the groups, renders precise comparisons of the 24 hour outputs of aldosterone statistically questionable. This relatively mild sodium restriction did not produce the 300 per cent increase in steroid excretion reported in normal males.

These findings on identification and quantitation of aldosterone, however, shed some light on the determinations of sodium-retaining activity recorded above. Since the antepartum care in this clinic (and in most others) includes some restriction on the consumption of the sodium ion, all of the "normal pregnant" women assayed had received such instructions and had followed them with variable degrees of faithfulness. It is, indeed, doubtful that any of the cases reported to date have not had some degree of sodium restriction imposed prior to being classified as toxemic.

D. Potassium loading: The possibility that aldosterone appears in response to the necessity for eliminating potassium requires consideration.

Leutscher²⁹ does not record the potassium content of the diet which in his subjects led to the urinary elaboration of aldosterone, while Laragh and Stoerk³⁰ have reported that dogs on sodium restriction will produce significant amounts of this steroid only in response to the administration of potassium.

Accordingly, a group of women in the last trimester were admitted to the Balance Ward and maintained on measured diets for a period of 7 days. These women were hospitalized in pairs and freely permitted sodium while the potassium intake was limited to 2 Gm. a day, but in addition one of each pair received a potassium supplement orally of 4 to 4.5 Gm. a day. As additional controls for these studies and for the sodium restriction group ("C" above), the urines from 8 women with pre-eclampsia were chromatographically fractionated and assayed for the micrograms of aldosterone excreted per 24 hours.

The patients with pre-eclampsia produced on the average 20 micrograms of aldosterone per day. This average figure is actually not much greater than that reported for normal patients and provided a low base line for comparative purposes. In contrast, at the end of 5 days the potassium-loaded nontoxemic women showed no significant SRF in their urines. The pregnant patient appears to be moderately responsive to sodium restriction in elaborating this steroid, but an additional load of potassium in these experiments did not increase the degree of this activity in her urine.

These studies are incomplete to the extent that the test urines for fractionation and assay were collected only after at least five days of the administration of excessive potassium. Possibly 24 or 48 hours after the administration of this load the aldosterone assays would reveal an increase. The permutations of possible levels of sodium and potassium intakes and days of testing are almost limitless, and these studies are being continued.

Summary

This study confirms the fact that women with the eclamptogenic toxemias demonstrate a marked increase in the sodium-retaining activity of the urinary corticoids, but this is a statement true on the average. Individually some non-toxemic pregnant patients also demonstrate increased excretion of this factor, while some individual toxemic women show no such change. Diuresis diminished the amount found, although in all other respects the patient's clinical picture may have remained the same; by our technique of measurement it had disappeared from the urine after the third postpartum day in all cases. Placental extracts did not contain a strong sodium-retaining fraction.

Chromatographic quantitations of aldosterone have indicated in this group of normal pregnant women a higher range than reported for the nonpregnant. Attempts to increase this factor by the administration of steroids were unsuccessful. The results with prolonged ACTH in a small group of women were not conclusive, but certainly cannot be called finally negative. Also, the pregnant woman in the last trimester responds to sodium restriction with some increase in the urinary aldosterone. Finally, adding a potassium load has not as yet demonstrably increased the excretion of the sodium-retaining factor. This steroid—the most potent of the sodium retainers yet isolated—has not been demonstrated to be the cause of the edema in the eclamptogenic toxemias and from the studies reported here could be a sequel as much as a

n p

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8

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cause of the syndrome. It undoubtedly forms a part of the normal mechanism for electrolyte control, and its role as an eliminator of potassium will require additional study of the metabolism of this ion in toxemia.

We wish to express our appreciation to Miss Ruth Wagner and Mr. Theodore Eickhoff for their technical assistance, and to Dr. Gordon Farrell who has given generously of his time in teaching the various techniques employed.

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Discussion

DR. ROBERT B. WILSON, Rochester, Minn.—It has been 25 years since the discovery of the high life-maintaining activity of adrenal extracts, 20 years since knowledge of an amorphous fraction having mineralo-corticoid activity became known, only a scant 2 years since the substance having this activity was crystallized, and but one year since its chemical constitution was determined and the name "aldosterone" given it.

We are fortunate that Dr. Barnes and Dr. Quilligan have so quickly and ably given us definitive information on the excretion of this substance in women with toxemias of pregnancy. Others have given us information on the excretion of the SRF but to my knowledge this is the first presentation on the excretion of aldosterone.

The history of obstetrics is intimately associated with research and theories as to the cause or causes of the toxemias of pregnancy. With the discovery of aldosterone and the knowledge that its main physiologic action is to cause the retention of sodium and the excretion of potassium and that it is found in the urine in increased amounts in clinical conditions associated with water retention, the hope arose that at last there might be a lead which would permit the discovery of the etiology of the toxemias. However, as the authors have shown, this is probably not the case. In all likelihood the increased excretion of aldosterone in the toxemias of pregnancy is a result rather than a cause of the syndrome. I could not be certain from reading the paper whether or not Dr. Barnes has any firm opinion in this regard and would like to ask him if he feels that an increase in the production and excretion of aldosterone is or is not the cause or one of several possible causes of the retention of sodium and water found in the toxemic patient.

With the variations in actual amounts excreted in each classification of the toxemias and with the lack of correlation as to the amount excreted as compared to the clinical severity of the toxemia, it is apparent that this endocrine substance behaves in an unpredictable fashion in individual toxemic patients, as do the estrogens, progesterone, and chorionic gonadotropin.

The authors have given some patients estrogens, progesterone, and cortisone and noted no increase in the excretion of the SRF. I wonder if any assays of the estrogens, corticoids, pregnanediol, or chorionic gonadotropin were done in the course of this study and if so whether there was any correlation between the excretion pattern of these substances and of the SRF. If such assays were not done, it might be worth while to do them in view of the well-known variations in the excretion of these hormones in some toxemic patients.

The experiments involving the administration of corticotropin (ACTH) to normally pregnant women has led the authors to state that they are "not inclined at the moment completely to dismiss ACTH as contributing to the mechanism of the production of aldosterone-like steroids in pregnant patients." Many other clinical and research investigations have seemingly established that aldosterone is secreted in the absence of the pituitary and that its secretion apparently is not controlled by corticotropin but probably is controlled by the electrolyte intake. Unless the electrolyte intake is controlled in such experiments and until more such patients have been studied I would think that this tentative conclusion of the authors might not be justified.

In any evaluation of the results of endocrine secretion and excretion in pregnant women, either normal or toxemic, so many factors which might influence this secretion and excretion are present that an adequate explanation of the physiologic or pathologic mechanisms seems, on the basis of our present knowledge, well-nigh impossible. For example, the production of any adrenal steroid involves a series of reactions in which the cortical elements start with one or more basic steroids and by biosynthesis produce the corticoids and the androgens. The steroids then produced are catabolized in the liver, kidneys, and other organs. Certainly, in the toxemic state, in which the pathologic changes in the kidneys and liver are so varied and in which normal physiologic processes are so disrupted, the explanation of a change in the excretion pattern of any adrenal steroid becomes most difficult. In view of these complexities, further basic knowledge must be obtained before our understanding of the physiology of any of the endocrine problems in pregnancy can be called adequate.

DR. E. STEWART TAYLOR, Denver, Colo.—It is natural that alert investigators would search for a relationship between abnormal sodium metabolism, pregnancy toxemia, and aldosterone. Aldosterone from the adrenal cortex is the principal electrolyte hormone from the adrenal, and is the most effective substance yet isolated for the maintenance of sodium and potassium balance. There appear to be two types of hyperaldosteronism, the primary and the secondary varieties.

Secondary aldosteronism occurs in a variety of conditions characterized by edema and low sodium excretion (hence the other name for this hormone, sodium-retaining substance). Pathological conditions associated with aldosteronism are nephrosis, heart failure, hepatic cirrhosis, pre-eclampsia, and malignant hypertension. It is thought that the increased excretion of aldosterone in these pathological entities is an effect, and not the cause, of the fundamental disease process. The authors agree with this concept.

Primary aldosteronism appears as a newly described syndrome. Conn (J. Lab. & Clin. Med. 45: 661, 1955) describes a patient who complained of intermittent tetany, parasthesias, polyuria, polydipsia, chronic severe muscular weakness, hypertension, and no edema. This patient had high titers of sodium-retaining substance in the urine, low blood potassium, high blood sodium, and alkalosis. There was a renal tubular defect in water reabsorption, probably secondary to the low blood potassium. Operation revealed an adrenal cortical adenoma that was rich in aldosterone activity. After operation the symptoms of hyperaldosteronism disappeared. The symptoms of hyperaldosteronism could be reproduced by the administration of small doses of aldosterone. Other similar cases have been reported. Such tumors are counterparts of adrenal cortical tumors which produce 17-hydroxycorticoids and cause Cushing's syndrome, and those which produce androgens and cause virilization of the female. Conceivably, an adrenal-like tumor of the ovary could produce the syndrome of hyperaldosteronism. No such metabolic type has been reported to my knowledge, although the latter two metabolic types have been reported though rare.

Drs. Barnes and Quilligan have shown that the sodium-retaining factor is generally increased but not always, in pre-eclamptic patients. They also have demonstrated that the degree of sodium retention does not bear a direct relationship to the severity of the pre-eclampsia. Their work, as well as that of others, appears to eliminate the placenta as the source of significant amounts of aldosterone. Most authorities believe that tropic hormones from the anterior pituitary gland are not necessary for the adrenal manufacture of aldosterone. The authors have presented what they consider as inconclusive but contrary evidence to the effect that during pregnancy ACTH does stimulate the adrenal cortex to produce more aldosterone. This needs more study.

The most novel part of the experiments reported today is that having to do with the feeding of excess potassium to pregnant patients. The results reported do not reveal that aldosterone is excreted in increasing amounts because of overdosage of potassium. This particular division of the experiment should be pursued further to help determine the relationship of this hormone to potassium metabolism.

The methods for determining the results in these studies have been carefully selected, and are excellent methods. The use of bioassay and paper chromatography for the checking of determinations is especially valuable. The authors have been careful to point out that they are not presenting conclusive evidence that what they are measuring is aldosterone, but that it is a salt-retaining substance which in all probability is aldosterone.

DR. EDWARD C. HUGHES, Syracuse, N. Y.—Facts and figures presented at this session of the Association, pertaining to the toxemias of pregnancy, add appreciably to the previously reported evidence that sodium and water and the adrenal steroids, in relation to one another, are perhaps causative agents in creating these pregnancy complications. Perhaps a correlation of these facts should be attempted although no conclusions can be drawn at this time.

In 1940 our group reported that serum sodium was at a lower level in the acute toxemias of pregnancy, but that the excretion of sodium in the urine was decreased. Tatum, in his paper the other day, showed this further in the statement that the tissue fluid retained excessive amounts of sodium in these complications. Dieckmann brought out an important point when he stated that the sodium levels of the skin were elevated in toxemia. If we consider the surface area of an individual, we can comprehend that there is a sizable storehouse for sodium in the skin.

Several years ago our group also presented before this Association some evidence that there is a moderate increase in the total excretion of adrenal cortical steroids in normal pregnancy, that this steroid, desoxycorticosterone, may regulate the balance of sodium and water in the acute toxemias. These determinations were done chemically and also by paper chromatography. We did not know at that time whether these substances came from the maternal adrenal or whether from the placenta. We still do not know this.

Dr. Barnes has presented good evidence that aldosterone, the most potent salt-retaining hormone, is increased in some of the toxemias.

We have also been working with aldosterone and we find it is a very difficult substance to determine. Dr. Charles Lloyd and Miss Lobotsky of our group have just published a method of determination of aldosterone in the serum. We find that it is present in some individuals, in about 0.08 gamma per 100 c.c. of blood. We also find it is increased in cirrhosis of the liver as Dr. Barnes has stated. We have not yet determined it in the toxemias of pregnancy. When we thought we had some evidence of the increased levels of a salt-retaining substance by paper chromatography, we tried to correlate that with the aldosterone and, on the chromograph, it does not come down at the same level as the aldosterone. That adds to the confusion a little more.

Dr. Barnes stated that the placenta did not contain increased amounts of aldosterone. This has been found by others. I wonder what role the fetus plays in this condition. We have been doing some work on the fetus in respect to 17-ketosteroids, and we find that in the fetus the level of these substances is elevated much more than in the mother, and in the premature it is higher yet. No work has yet been done on toxemic patients. Perhaps, if the placenta does not give cortisone to the mother, the fetus does. We do know that the fetus has enlarged adrenals at the time of birth.

At the time we reported the increased levels of total adrenal cortical steroids we noted also that the pregnandiol level was increased in pregnancy, a fact observed also by many others. We have now found that some of the pregnandiol, which we thought was the end product of progesterone, is actually pregnantriol. This is a different compound and may be associated with adrenal secretion.

I was also interested in the fact brought out by this paper that by elimination of salt, the output of the aldosterone is increased. To understand the mechanism of this, we should have serum levels.

What is the clinical application? As soon as the placenta is fully functioning at 4½ to 5 months, we should start to put a moderate restriction on salt intake. We have done this and I think it has paid off in respect to the incidence of toxemia, which has been lowered dramatically.

DR. EDWARD QUILLIGAN, Cleveland, Ohio.—Those results which have been reported, using the animal assay, actually show only the biologic activity of the corticoid extracted from the patient's urine. There have also been chromatographic results reported in which a spot, in approximately the proper location of aldosterone, has been identified as this steroid. Actually, we feel that one should perform both techniques in order to be able to state definitely that he has isolated this hormone. Using such techniques, we come to rather temperate results. In a time when aldosterone is being implicated as a cause of a great many clinical entities, our findings would be equally compatible with the thesis that it is the result of the pathologic changes in the toxemia, rather than the cause.

DR. BARNES (Closing).—To Dr. Hughes' statement that he would like to see the serum levels done, I would like to comment that we did not do this ourselves simply because it would be reduplication of Dr. Gordon Farrell's work now being carried on in our physiology laboratories. To be accurate this method requires such an amount of blood that he practically exsanguinates a dog from the adrenal vein to get the blood levels. Undoubtedly, simpler techniques for blood determinations will become available.

Dr. Taylor makes the point that this should lead us to more studies of potassium, with which we agree. It has been partly historical accident that we have been entranced by sodium retention, as sodium was the easier one of the two to determine initially, and its metabolism seemed a little more clear-cut. When a powerful steroid has the dual activity of retaining sodium and eliminating potassium, both aspects of this action should be considered.

Dr. Wilson raises a point on the electrolyte control in those patients who were involved in the ACTH experiment. His point is perfectly valid. The lability in patient response to sodium restriction means that, to be believed, most pregnant subjects would have to be admitted to a balance ward and to have their sodium intake controlled. He asked if we did other assays in the group to whom steroids were administered. No, we did not, but the normal males who received ACTH in the experiments reported by Luetscher had other urinary steroids assayed and there was no fixed relationship between them the aldosterone that they put out.

Finally, he asked if I would cast a public vote as to whether or not aldosterone is truly etiological in pre-eclampsia. I do not think that it is the cause of toxemias. I do not think it is even proved to be the cause of the edema of the toxemis although its excretion in the urine is an almost universal finding in the edematous pre-eclamptic patient.

THE RATIONAL TREATMENT OF THE PATIENT WITH PLACENTA PREVIA*

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(From the Texas Postgraduate Medical School)

M Y INTEREST in placenta previa was aroused very suddenly, dramatically, and tragically. In May, 1919, on the threshold of graduating from medical school, and having decided to enter the field of obstetrics, I witnessed the handling of the following case on the obstetrical service of a large teaching hospital.

Mrs. M. B., white, a multipara 21 years of age, eight and one-half months pregnant, was admitted to the hospital because of profuse vaginal bleeding. She had reported episodes of bleeding three days previously and had been instructed to remain in bed. Upon her arrival at the hospital, a Voorhees bag was inserted through a cervix dilated to 4 cm., and the bleeding stopped. Stimulants were given and proctoclysis started. The patient died three hours later, undelivered. Autopsy showed placenta previa.

One can readily understand that this incident, occurring so early in one's medical career, would stimulate a natural desire to become acquainted with the most successful method of treatment of this grave condition.

In reviewing the measures employed in the management of placenta previa over the past century, one is impressed with the changes which have taken place. In 1849, Charles D. Meigs,⁵ of Philadelphia, wrote a textbook in which he discussed placenta previa as follows: "A flow of blood, more or less violent, ensues, but stops as soon as the patient lies down or makes use of venesection or some cooling drink. These attacks of bleeding are renewed again and again, and are denominated the unavoidable hemorrhage." He advised that, in order to protect the patient, the services of another medical practitioner be retained for all sudden emergencies during the absence of the regular attendant. The practice of accouchement forcé was condemned by this author, and the profession was reminded, "It is the loss of the last half pint of blood that kills the patient." Meigs likewise called attention to the newer method of treatment, advocated by Drs. Simpson, Radford, and other eminent brethren in England, which consisted of the "total separation of the placenta by the hand of the accoucheur," and was regarded as "a certain method of putting a stop to the effusion of blood." It is now difficult to realize the sad state of obstetrics at that date. How desperately the profession was grasping for a solution to this serious problem!

Seventy-five years later, in his textbook of obstetrics, published in 1924, Williams⁷ referred to the work of Poerter, Van Herff, Strassmann, and Hof-

^{*}Presented at the Sixty-sixth Annual Meeting of the American Association of Obstetricians and Gynecologists, Hot Springs, Va., Sept. 8 to 10, 1955.

meier in regard to the treatment of placenta previa. At that time, Williams favored the use of the balloon as well as the Braxton Hicks version, and stated, "Thus far, only two cesarean sections have been done on our service for placenta previa." Today, neither the balloon nor the Braxton Hicks version has more than a meager place, if any, in the management of this condition. Although I have had no experience with the Willett clamp, I wonder if it might not be placed in the same category.

From the small number of cases of placenta previa which I have observed during my 33 years in obstetrics, it is clear that experience with this condition in private practice is limited. Of a total of 10,059 personally conducted deliveries during this time, only 60 cases of placenta previa have been definitely diagnosed by vaginal examination or at the time of cesarean section. This constitutes an incidence of 1 in 170. If placenta previa were not so often the cause of abortion, as shown by Javert,² no doubt the incidence would be much higher.

In an analysis of this small group of cases, several previously known facts concerning placenta previa were corroborated. The incidence was higher in older patients, 35 of the 60 having been over 30 years of age and 17 of these over 35 years. Only 18 were nulliparous, while 42 were multiparous. As one would expect, the incidence of breech and other abnormal presentations was exceptionally high. Vaginal bleeding first appeared before the eighth month of gestation in over half the 60 patients. None had any hemorrhage after the date of expected confinement. In view of these findings, the expectant mother, at the time of quickening, should be warned of the danger of bleeding and advised as to the immediate measures to be taken should this contingency arise.

During the nineteen-twenties, the use of the Voorhees bag and the Braxton Hicks version were the accepted forms of treatment for placenta previa. Eight patients of this group, who were observed during that period, were treated by these procedures. All of the mothers survived and 7 live, uninjured infants were delivered. The heart sounds of the remaining infant had ceased before the Braxton Hicks version was performed. Not until 1943 did I use a Braxton Hicks version again, and then only as an emergency measure for placenta previa with prolapse of the cord. The outcome was successful, but because of the difficulty of holding the leg of an infant for several hours to control bleeding while the cervix slowly dilates, as well as having a balloon break occasionally, one can readily understand why this method has become outmoded.

From the standpoint of management, cases of placenta previa may be divided into two groups: (1) those in which the fetus is apparently viable and (2) those in which its viability is questionable or has not been attained. If one is certain of viability, one of two methods may be employed: (1) if the bleeding is moderate and labor has advanced sufficiently, amniotomy will fer an excellent outcome for both mother and infant; (2) if bleeding is proncured and the continuation of labor will result in further hemorrhage and consequent danger to mother and child, I feel that cesarean section is definitely indicated. In order to determine which of the two courses to pursue, a vaginal examination is necessary. This should be made with extreme caution. Prior to the examinaiton, one should be prepared to interfere promptly and should be certain of having available sufficient blood for replacement.

In an excellent contribution, Parks and Barter⁶ suggested a clinical classification of the different types of placenta previa and discussed the neces-

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sary safeguards for its successful management. The complacency with which Johnson's regards placenta previa has helped to dispel fear in the minds of the profession and to prevent hasty interference. However, the so-called conservative treatment by vaginal delivery and frequent or continuous blood transfusions which he recommends, without adequate preparedness for intervention, if indicated, seems fraught with danger. It is recalled that Bill,1 at an earlier date, showed conclusively that transfusions before as well as during operative intervention will materially improve the results in these cases.

In 47 of the 60 cases comprising this study the fetus was viable. The methods of management and results in the 47 cases are shown in Table I.

TABLE I. TREATMENT AND RESULTS IN 47 CASES OF PLACENTA PREVIA WITH VIABLE FETUS

	NO. OF		MORTALITY			
SERIES	CASES	METHOD OF DELIVERY	MATERNAL	INFANT		
A	9	Braxton Hicks version or Voorhees bag	0	1		
\mathbf{B}	16	Amniotomy (2 cases) Breech decomposed	0	0		
C	21	Cesarean section	1	5		

Note.—One other patient had a spontaneous prolapse of the placenta and cord. Delivery was successfully accomplished by podalic version.

In Series A and B, labor had been definitely established when the bleeding began and the placenta was marginal or lateral. In Series C, wherein cesarean section was performed, the placenta for all practical purposes covered the greater area around the internal cervical os. Two of the fetal deaths were unavoidable, one having been due to an encephaly and the other to erythroblastosis fetals. Only one possible explanation has been found for the other 3 fatalities. MacFee, in 1945, showed that at the time of cesarean section the life of the infant is in danger because of the thinness of the placenta, the location of the insertion of the umbilical cord, and the loss of blood should the incision be made through the placental site. The deaths of the 3 viable infants, all apparently normal according to autopsy studies, must be attributed to a complication related to one or more of these dangers.

The Rational Treatment in Cases of Borderline Viability of the Fetus.— In medicine, a departure from accepted opinions or practices, especially in regard to lifesaving procedures, is generally prompted by some profoundly impressive experience. Formerly, it was the general concept that, once a diagnosis of placenta previa was made, immediate steps should be undertaken for delivery, since the patient was considered to be "sitting on a keg of dynamite." Two personal experiences led me to differ from this view and were largely responsible for the policy which I have pursued in 13 cases of placenta previa observed since Doubtless, this plan is not original; probably other obstetricians have followed a similar one throughout the years, since it is the most rational means of obtaining a satisfactory outcome for both mother and infant.

In 1924, I was called by Dr. J. Allen Kyle, of Houston, to see in consultation a primiparous patient who was approximately six lunar months pregnant. She had suffered several episodes of vaginal bleeding during the previous two months and the diagnosis of placenta previa was clear. The patient was opposed to the institution of any radical measures at this early stage. I was informed by Dr. Kyle that he had observed similar cases in the hospital on several occasions and, despite many episodes of bleeding, the mother and infant were ultimately brought through the difficulty successfully. With this assurance, and since Dr. Kyle lived adjoining the hospital and both he and I would be available in an emergency, the patient was permitted to continue her pregnancy. A live, healthy

girl, weighing 6 pounds, was delivered by cesarean section. This experience convinced me that a course of watchful waiting while being prepared for any emergency was the rational one.

The second of these two cases was interesting because of its rarity. In December, 1925, a physician in a town 60 miles away called and stated that he was sending by train a patient who was a multipara at term. She had had a moderate amount of painless bleeding which he had diagnosed as placenta previa. Before her departure, he administered morphine, ½ grain. She was met by ambulance and brought to the hospital, where I saw her in the delivery room immediately. While she was en route, the bleeding was moderate and intermittent. During preparations for a vaginal examination, the entire placenta and cord prolapsed from the vagina simultaneously with the rupture of the membranes. The patient was given chloroform and a live male infant, weighing 7½ pounds was delivered by podalic version. This almost unbelievable incident provided further assurance that the patient with placenta previa can endure many episodes of bleeding and that the infant likewise withstands blood loss well. In this case, the salvaging of the infant was quite unexpected.

Table II shows a summary of the 13 cases in which I have followed the rational method of treatment.

TABLE II. THE RATIONAL METHOD OF TREATMENT IN 13 CASES OF PLACENTA PREVIA

CASE		LENGTH OF HOSPITAL	WEIGHT OF INFANT	MORTA	ALITY
NUMBER	PARITY	STAY	(POUNDS)	MATERNAL	INFANT
1	Primipara	24 days	6	0	0
2	Primipara	6 weeks	5846	0	0
3	Multipara	17 days	52/16	. 0	0
4	Multipara	2 weeks	54/16	0	0
5	Multipara	4 weeks	43/16	0	0
-	•	(2 weeks at home)	7.20		
6	Primipara	4 weeks	7	0	0
	*	(3 weeks at home)			
7	Primipara	4 weeks	45/16	0	0
8	Primipara	30 days	6	0	0
9	Multipara	3 days	38/16	0	0
10	Multipara	12 days	61/16	0	0
11	Primipara	7 days	44/16	0	0
12	Multipara	10 days	24/16	0	0
13	Primipara	7 days	28/16	0	1*

*Died first day; spontaneous breech delivery.

The wisdom of allowing the patient who has had episodes of bleeding to remain at home while an attempt is being made to gain viability of the fetus is open to question. Such factors as parity, the intelligence and economic situation of the patient, and accessibility of the hospital must be considered. MacFee⁴ states that it is unnecessary to keep the patient in the hospital for suspected placenta previa. In two of my cases I compromised in this matter by allowing the patients to return home after several days in the hospital.

Since all the 13 patients treated by this method had many episodes of bleeding, one is forced to conclude that the pregnant mother and her child can withstand frequent losses of blood surprisingly well, and that the first hemorrhage rarely has to be dealt with as an obstetrical emergency. It is obvious, also, that vaginal examination can be made without provoking hemorrhage.

Unfortunately, few are the cases in which the rational form of treatment is feasible. Every patient in this group cooperated fully in the treatment, yet 5 of the number bled so profusely, probably from impending labor, before

the lapse of two weeks in the hospital, that measures had to be taken to cope with the condition. Twelve patients had cesarean sections, and all the infants survived. The one death was that of an infant that weighed 21/2 pounds, delivered spontaneously as a breech presentation. The mother had been in the hospital for one week before delivery.

Comment

These experiences with placenta previa leave no doubt that maternal deaths may be prevented almost without exception, and the fetal mortality materially reduced, provided the physician observes a few rules in the conduct of the case and the patient cooperates fully in the treatment.

The obstetrical patient should be urged to carry out measures to keep her blood count and blood volume within normal limits during pregnancy. Soon after quickening, she should be informed of the significance of any vaginal bleeding and instructed as to the importance of remaining in bed should it appear.

Once bleeding begins, a soft tissue roentgenogram is useful for determining the location of the placenta. Even more important is the information obtained from fetograms as to the viability and any abnormality of the infant.

When an attempt is being made to obtain viability or additional development of the fetus, one is obligated to have some other physician constantly in readiness to proceed if emergency measures become necessary.

Cesarean section should never be undertaken without a careful preliminary vaginal examination to establish the diagnosis. Since time is of the essence in such cases, the availability of sufficient quantities of matched blood for transfuson offers considerable insurance against maternal mortality. The wise use of hypertensive drugs in the presence of shock is likewise an indispensable safeguard.

If indicated, cesarean section is preferably performed according to the classical technique, in that the danger of trauma to the placental site and consequent loss of the infant's blood is thus minimized. Also, the placenta may be more carefully separated from the lower uterine segment. separation, it is wise to attempt to give the infant more blood by gravity or milking of the cord.

One cannot overestimate the danger attending low implantation of the placenta. In 4 of the cases in this series an unplanned hysterectomy was necessary at the time of cesarean section because of uncontrollable bleeding at the placental site.

A concentrated residency program, bolstered by the teachings of an experienced staff, is of inestimable value as a means of providing experience in the management of placenta previa. In the majority of cases the outcome is successful, yet it behooves us to remember that this is a grave complication and one which requires our greatest sagacity. Maternal deaths still occur, although in the current era success is usually judged by fetal salvage.

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Discussion

DR. NEWLIN F. PAXSON, Philadelphia, Pa.-Dr. Johnston has demonstrated the success which follows the use of skill and good judgment in the treatment of a major obstetrical complication. Sixty cases, with one maternal death, a gross fetal loss of 7 and a corrected loss of 4 gives the very low maternal mortality rate of 1.6 per cent and the corrected fetal loss of 6.6 per cent.

This record is in keeping with the trend of improved obstetrics. Analysis of Philadelphia's maternal deaths for the five-year period of 1950 through 1954 shows only 8 cases of fatal antepartum hemorrhage, including both abruptio placentae and placenta previa.

We have developed a plan of management at Hahnemann Hospital similar to Dr. Johnston's, based on the belief that the four chief factors that affect judgment in the management of placenta previa are: (1) degree of bleeding, (2) location of the placenta, (3) condition of the cervix, (4) duration of pregnancy.

Active bleeding and total placenta previa have first priority and require immediate delivery-cesarean section. With slight, or intermittent, bleeding and an effaced, ripe cervix, amniotomy with or without Willett forceps is used, provided the fetus is viable, near term, or labor has started.

With slight bleeding and a nonviable or very premature fetus, careful observation is permitted with blood replacement by frequent small transfusions. Pregnancy, however, is terminated on any danger signs, such as persistent bleeding or anemia, and usually by cesarean section.

I am in strong agreement with Dr. Johnston's insistence on a careful digital vaginal examination when placenta previa is suspected. With proper skill and gentleness these examinations can be done successfully and without damage to the pregnancy. They are needed for an accurate diagnosis.

Usually I have used the low segment cesarean section in these cases, as Dr. J. B. DeLee advocated more than twenty-five years ago. Bleeding points can be clamped by ring forceps or T clamps under direct vision and, in my experience, a cesarean hysterectomy has not been necessary to control postpartum hemorrhage. The advantage of the low segment incision is the stronger scar with less danger of rupture in future pregnancies.

When one of these women who has cesarean section for placenta previa becomes pregnant again she does not have a repeat cesarean section performed on her, but is permitted to deliver through the birth canal as long as all other factors are normal.

DR. J. P. GREENHILL, Chicago, Ill.-Johnston and his former associate Herman Johnson, as well as MacFee, were pioneers in advocating a waiting policy in selected cases of placenta previa. They definitely proved that many babies can be saved without harm to the mothers by temporizing. Before this the almost universal treatment of placenta previa was to empty the uterus as soon as the diagnosis was made, without jeopardizing the mother, regardless of the viability of the baby. Now, almost everywhere, women who have placenta previa with a nonviable baby, and who do not bleed profusely, are permitted to continue their pregnancy until the baby is definitely viable, unless new and profuse bleeding episodes make emptying the uterus imperative.

It is important, of course, to be certain that a woman who bleeds late in pregnancy has placenta previa, and not some other cause for the bleeding. This is accomplished by either a careful vaginal examination, x-ray visualization, or both procedures. It is important to remember that rupture of the marginal sinus is an important cause of such bleeding, as emphasized by the Bartholomew group. In fact, placenta previa is the cause of painless bleeding in only about one-third of such hemorrhages.

I agree with Johnston that there should be only two forms of therapy for placenta previa: (1) rupture of the membranes, and (2) cesarean section. I am opposed to the use of bags and Hicks version just as is Johnston. Conservative treatment should be used in women who have not bled much and who have partial placenta previa. Cesarean section should be done in all women with total placenta previa and those who bleed excessively regardless of the condition of the baby, particularly if the cervix is not effaced and partially dilated.

During a cesarean section for placenta previa it is most important to try to avoid cutting through the placenta. When the placenta is cut and it often must be when a low cervical operation is done, the cord should be clamped immediately after making the uterine incision and before delivery of the baby. This is to prevent severe loss of the infant's blood and shock in the infant. Much of this danger can be removed by performing a classic cesarean section as advocated by Johnston. Anemia in the newborn is not infrequent in babies born of mothers with placenta previa. Hence every baby born in cases of placenta previa and also in cases of abruptio placentae should have repeated blood studies after birth.

It is needless to add that the mother's blood must be saved at every step and blood transfusions given when needed and in sufficient amounts. On the other hand, blood should not be given unless it is really necessary. There are too many complications after blood transfusions particularly hepatitis.

We should be grateful to Johnston for his final emphasis, namely, that even though the results for mothers and babies are far better than they were only a few years ago, we should not look upon placenta previa with complacency, even though Herman Johnson properly toned down the extreme fear with which placenta previa was formerly regarded.

DR. JOHNSTON (Closing).—The one maternal death in my series must be considered as avoidable, with the responsibility resting on the attending physician. Since a cesarean section usually involves a loss of 300 to 500 c.c. of blood, it is mandatory that more than the usual blood replacement be held in readiness in these cases. The choice of the anesthetist, as well as the selection of the hospital with its associated laboratory facilities and personnel, falls into the realm of responsibility of the attending accoucheur.

In conclusion, may I again emphasize my clinical impression that in order to minimize loss of blood in the premature infant every precaution should be made to avoid an incision through the placental site. In such cases where it is unavoidable, immediate transfusion of the baby may be a lifesaving procedure.

Department of Reviews and Abstracts

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Review of New Books

Antenatal and Postnatal Care. By F. J. Browne and J. C. McClure Browne. Eighth edition. 672 pages with 88 illustrations. Boston, 1955, Little, Brown & Company. \$4.90.

The authors have written another edition of an obstetric text that has found favor in London since 1935.

The chapter on the influence of the emotions upon pregnancy and parturition written by G. D. Read is concise and instructive.

Incomplete abortions are treated by the administration of hot intrauterine douches following the uterine curettage. The therapeutic value of the douche is certainly open to question. Curettage is advised as a method of diagnosis for extrauterine pregnancy. There is a definite danger, however, that the gestation may be intrauterine and no histologic information derived from the procedure is diagnostic. The authors state that in tubal pregnancy the abdominal pain is severe and cramplike and precedes bleeding, whereas in intrauterine abortion bleeding is the initial symptom and then abdominal pain occurs. In the management of eccyesis, transfusions are not advised preoperatively because of the fear that fresh bleeding may occur intra-abdominally. They claim good results in selected cases of extrauterine pregnancy by expectant nonoperative treatment.

The chapter on the Rh factor and erythroblastosis is complete and the differentiation from hemolytic disease caused by ABO incompatibility is made.

The section on toxemia of pregnancy is a good review of the subject and one to which the authors have made several contributions.

The discussion of the medical complications of pregnancy is excellent. The role of mitral commissurotomy in valvular mitral stenosis in early pregnancy is cited.

The treatment of contracted pelvis by the induction of premature labor is a peculiarly English method that has not found favor in America or in the Continental clinics. Rupture of the membranes at the end of the thirty-seventh week by means of a Drew Smythe catheter or a solid rubber bougie is practiced. Admittedly many unnecessary inductions are carried out because it is often difficult or even impossible to assess accurately the degree of disproportion or, indeed, whether disproportion is present at all.

The use and value of radiology in obstetrics are authoritatively treated by J. Chassar Moir, and the x-ray reproductions are good. The discussion of postnatal care is limited to 14 pages.

The book does not contain many references to the current medical literature. It is of value to those interested in some of the obstetric practices in many of the medical schools and hospitals in London and has been written primarily for general practitioners and medical students.

Clinical Research in Diabetes and Pregnancy. Edited by Jørgen Pederson. 350 pages. Papers from the Lying-In Hospital, Copenhagen, 1954.

This excellent monograph represents the work done by the Danish school in regard to diabetes and pregnancy. It covers not only obstetric but also pediatric and medical

management of the pregnant diabetic patient. Although these papers have been individually published previously, this monograph is highly recommended to all who are interested in the care of the pregnant woman with diabetes. All aspects of this problem have been placed in one volume.

Uber den Einfluss der Schwangerschaft auf die Lungentuberkulose. By Klaus Obmann. 142 pages with 216 illustrations. Leipzig, 1955, Georg Thieme. DM 25.

The author has added 142 more pages to the voluminous literature on this highly important but yet unsolved question of the relationship between pregnancy and pulmonary tuberculosis. Most of the book consists of the case histories of 347 women with tuberculosis, and the 531 pregnancies experienced by these women. The more complicated cases are illustrated by graphs. Only 13 of the 216 figures are prints of x-rays.

The last 22 pages of the book are concerned with a critical discussion and statistical analysis of the material. The author has spent a great deal of effort to indicate exactly, by number, which cases are concerned in any group or classification of the analysis so that the reader may evaluate for himself the validity of any group.

He makes a plea for more frequent x-ray study both during pregnancy and in the year following a pregnancy to effect earlier diagnosis and treatment. He also feels that the indications for therapeutic abortion on the basis of pulmonary tuberculosis should be strictly limited but that in certain selected cases a definite indication exists.

The fact that so few of the patients were treated with the latest antituberculosis drugs, viz., streptomycin, PAS, and isonicotinic acid hydrazide detracts from the value of this study in terms of the effect of the pregnancy on pulmonary tuberculosis in a patient undergoing modern chemotherapy. Therefore, this small book is, unfortunately, of little aid to the practicing obstetrician treating such cases.

Midwifery. By F. W. Roques. Ninth edition. 607 pages with 249 illustrations. Baltimore, 1955, The Williams & Wilkins Company. \$7.00.

Written primarily for medical students and young practitioners, the book expresses the collective view of ten contributors, all of whom have been actively engaged in teaching obstetrics in the medical schools of hospitals in London.

Apparently early ambulation as defined in America is currently not practiced in London. The patients are permitted out of bed on the fifth postpartum day and remain in the hospital for approximately fourteen days.

Pre-eclampsia is defined by the British clinicians as the variety of toxemia in which edema, hypertension, and albuminuria develop late in pregnancy. The control of convulsions in eclampsia is mainly through sedation with chloral hydrate and morphine although other drugs including magnesium sulfate and Veratrum preparations are mentioned.

In the treatment of threatened abortion it is advised that the patient should be kept in bed for five days after bright red bleeding has ceased but that the loss of dark blood is of no importance. No rational explanation for this attitude is given. The current therapy for habitual abortion consists of implantation of progesterone pellets but its value has recently been questioned by Swyer in London. In the book it is stated that the chances of a patient's carrying a pregnancy to term following three consecutive spontaneous miscarriages is only 15 per cent. In view of recent evidence the statement is no longer valid.

The authors state that if diabetes mellitus complicates pregnancy delivery is effected at the thirty-sixth week of gestation or earlier by cesarean section in the interest of the fetus. Abdominal delivery is preferable to induction of labor.

Primary uterine inertia occurs in the first stage of labor and patients are allowed to continue in this state for several days. Apparently no untoward effects on the mother or fetus occur. Intravenous Pitocin is employed for the hypotonic type of primary inertia when it has been present for 24 hours or more. The hypertonic type of primary inertia

is treated best by reassurance to the anxious primigravida. Sedation, which gives the patient relief and rest, may eventuate in dilatation of the cervix. Oxytocic drugs are contraindicated in hypertonic primary inertia because of the tendency toward occurrence of a contraction ring or tonic uterine contraction.

Secondary uterine inertia occurs in the second stage of labor and is treated in two ways: (1) rest for the patient for 3 or 4 hours with sedation; (2) anesthesia and forceps delivery.

External cephalic version for a breech presentation is performed only under deep anesthesia with complete relaxation. The manipulation under these conditions would seem to entail a larger risk for the mother and fetus. Cesarean section for face presentation is deemed necessary only when a complication such as a contracted pelvis or prolapsed cord is present. Mentum posteriors are readily rotated and extracted with forceps.

The discussion of antepartum and postpartum hemorrhage is good.

The text is written in a straightforward manner and although no references are given the subject matter is covered fairly well. Many of the attitudes expressed do not coincide with current American obstetric practice. The discussions in general are good, however, and the policies appear sound.

It is a valuable book to possess for a succinct analysis of obstetric practice in London.

Perinatal Mortality in New York City. By Schuyler G. Kohl. 112 pages. Cambridge, Mass., 1955, Harvard University Press. \$2.50.

Concern over seemingly high fetal and infant mortality rates has been responsible for investigation in several cities of conditions associated with pregnancy, labor, delivery, and early infant care. This has been done in the hope that by discovering causes directly or indirectly related to a fatal outcome, ways could be found to prevent or ameliorate the responsible conditions.

The study in New York was carried out in 1950 and 1951, and the present volume is an analysis of these data. It was decided to investigate a random sample of 250 still-births, 500 deaths in the first month of life, and 250 from one month to one year. Investigators entered data on obstetric, pediatric, pathologic questionnaires and on a summary sheet. Later a code sheet was devised to which these data were transferred and this material was put on IBM cards to facilitate tabulation.

Part of the data was reviewed by a committee and part was directly evaluated by Dr. Kohl, who prepared the report. He has done an excellent job with the material with which he was presented, having had no part in planning the study. He has prepared adequate tables and carefully described the findings.

The material is extremely valuable but, unfortunately, not for the purpose for which it was intended. It states: where the infants who died were born, the general qualifications of the attendant at the delivery, maternal age, the parity and outcome of previous pregnancies, variety of anesthesia and analgesia used during labor and delivery, method of delivery, age at death, cause of death, and, in very general terms, who or what was responsible for the death.

It states that 65 per cent of the deaths were nonpreventable but that only 55 per cent were "unavoidable disasters," that house staffs had a higher preventability rate than obstetricians, and that nonteaching hospitals had a higher rate than teaching hospitals, that previous abortions were most frequent among mothers of infants who died in the early neonatal period, and that toxemias of pregnancy occurred with equal frequency among mothers of premature and mature infants who failed to survive.

The findings are extremely generalized and contribute little that has not been known previously. About all one can conclude is that mortality rates would be lower if doctors were better trained, if hospitals were better equipped, and patients were more cooperative.

The principal value of this report is to draw attention to the difficulty encountered in attempting to obtain meaningful data. A lack common to both this and the Chicago study is data on surviving infants. Knowledge concerning the significance of conditions

occurring during pregnancy and parturition in relation to nonsurvival, and information as to their frequency in pregnancies that end with surviving infants must be available. If causes of death are to be studied, autopsies must be performed and in this report only 35 per cent of the fetuses or infants were examined post mortem. A great indictment of the pathologists is Dr. Kohl's statement that invariably the committee making the study had to decide why the infant died because the protocol contained only a description of organs and never a statement as to the cause of death.

The investigators found records extremely incomplete; it was impossible, for instance, to evaluate prenatal care in 40 per cent of the cases because of lack of information. Records were inaccurate; among ten items on birth, death, or stillbirth certificates which were investigated there was an appreciable disagreement with clinical data in 2.3 instances per death.

They learned that data should be taken from charts by a thoroughly trained person and that this should be checked by an equally trained person; that the same panel should draw whatever conclusions are necessary on all cases, and not only on a selected few, and that the same panel should function throughout the study. It is also very evident to the reader that a study must be very carefully planned before it is commenced. A code sheet should be prepared in advance of the sheet on which data are to be transcribed and should be constantly available to the worker in order that no desired information is omitted if present on the chart.

Other communities undertaking studies of causes of infant death are certain to be greatly aided by this report.

The Plasma Proteins in Pregnancy. By Harold C. Mack. 110 pages with 22 figures. Springfield, Ill., 1955, Charles C Thomas, Publisher. \$3.75.

Studies of plasma proteins by their electrophoretic separation into true chemical entities were made in normal pregnancy, toxemia of pregnancy, in the mother and the fetus.

The alterations of the various albumin and globulin fractions were found to be largely quantitative. In the toxemias of pregnancy the trends in plasma protein composition, already apparent throughout the course of normal pregnancy, appeared to be further accentuated.

The plasma protein composition of the fetal blood in both normal and complicated pregnancies revealed that the fetus successfully achieved identical supplies of the various protein fractions despite the maternal dysfunction.

The material is presented in a lucid fashion. After reading the book, clinicians should have no difficulty in obtaining a clear insight into the various phenomena which the plasma protein fractions exhibit during gestation.

Sexual Hygiene and Pathology. By John F. Oliven. 481 pages. Philadelphia, 1955, J. B. Lippincott Company. \$10.00.

This is a timely and intensely practical book which fills a real need. There is no other modern text in English relating to sex matters to which the medical student and practitioner can turn. In modern times we have been negligent both in our teaching and in our research regarding human sexuality. Medical interest in these problems so evident a generation or two ago has given place to tacit acceptance without either understanding or very deep knowledge. The average medical course concerns itself but little with these problems and the practitioner goes forth with little better than lay knowledge tempered by a bit of folklore and perhaps some superstition. Kinsey has attempted, through sampling techniques, to tell us what the sexual mores of our current society are really like. He has come up with interesting and informative data but they do not really bring the picture of sexual function clearly into focus so that the learners and practitioners of medicine can cope with day-to-day problems.

Oliven has attempted to accomplish just this, in this text. He brings a life-long experience in both the psychiatric clinics of a large city hospital and the private service of the Columbia-Presbyterian Medical Center. This book moreover is not replete with psychiatric falderal, but is written in a simple, direct style. While aimed primarily at the practitioner there are enough theoretical data and sufficient emphasis on the unknown to stimulate interest and to give an adequate reference text.

Space does not permit any detailed description of the broad scope of this book, but mention of a few parts may be indicative. Divided into four sections, namely, Sexuality in Childhood, Sexuality in the Second Decade, Sexuality of the Normal Adult, and Sexual Pathology, the book contains many informative chapters. Those on childhood are particularly thorough and contain data on sex education, domestic nudity, sex aggression, and so forth, which would be difficult to find elsewhere. In the second section there is a particularly worth-while chapter on sex problems of the adolescent with items on petting, pornography, and masturbation. The section on adult sexuality discusses premarital counseling, problems of intercourse, contraception, marriage counseling, and divorce. The section on Sexual Pathology is concise and clear.

This book is not overdocumented, containing in all about 150 references. The one surprising thing to this reviewer is that the factual data obtained by Kinsey are referred to only once in the chapter on masturbation.

A Textbook of Physiology. Edited by John F. Fulton. Seventeenth edition. 1275 pages with 600 illustrations. Philadelphia, 1955, W. B. Saunders Company. \$13.50.

For most of the twentieth century this text has been used in many medical schools. The new edition contains many revisions and the first seven chapters on nervous function, as well as those on respiration, body fluids, and kidney function have been completely rewritten. (In the last-named chapter the author enters his wholly gratuitous disagreement with Homer Smith's mechanistic outlook.)

Specialists may criticize details, including diction and grammar, but this does not detract seriously from the great value of so well-established a textbook.

Vaginal Hysterectomy. By Laman A. Gray. 137 pages with 31 illustrations. Springfield, Ill., 1954, Charles C Thomas, Publisher. \$4.75.

This monograph in the American Lecture Series deals with the indications for and the technique and complications of vaginal hysterectomy. It is well written and the full-page illustrations are excellent. A new approach to closure of the vaginal vault is introduced which appears to be anatomically sound, simple in manner, and a step forward.

In the words of the author, the purpose of the book is to teach how to perform vaginal hysterectomy successfully. It does not miss its mark.

Gynaecology. By D. H. MacLeod and C. D. Read. Fifth edition. 864 pages with 551 illustrations. Boston, 1955, Little, Brown & Company. \$16.00.

The authors of the new volume are men of repute and vast experience in the field of gynecology. They have made many valuable contributions to the progress and development of their specialty. Both men enjoy a prominent position in medical literature. Hence, the publication of *Gynaecology* was looked forward to with great anticipation.

The introductory chapters on anatomy and physiology are quite well done. Thereafter, this voluminous fifth edition of MacLeod and Read is somewhat of a disappointment. Although practically every aspect of gynecology is covered, many sections are very sketchy and non-specific. The quality of the illustrations varies a great deal. In some chapters, they are excellent, in others, their clarity leaves much to be desired.

For the student of medicine, the volume is weak in organization and development of subject material. As an example, carcinoma of the vulva is briefly covered in a few pages

without adequate description of the pathology and course of the disease. The problem of therapy is passed over in a few sentences without statement of techniques, advantages of one modality over another, end results, and other important features of vulval malignancy.

There are no bibliographies which the reader might use to investigate a particular subject in greater detail. Although authors are quoted in the written text, there are only a few references as to the source of the quotation. Almost all of the suggestions to "further reading" are limited to papers in either the English or American literature.

For the specialist in the field of gynecology, this book offers very little because of the superficial and dated presentation of treatments and end results. On the use of radium in the therapy of uterine malignancy, the authors speak of dosage in terms of milligram hours in describing the "Paris Method" and in roentgens in the "Manchester Method." The reader might assume that these terms are interchangeable. In relating end results, there is no apparent consideration of factors that determine statistical significance. The authors admit the incompleteness of the chapter on gynecological operations, in view of which, this reviewer wonders whether it might not have been omitted. One finds many dated statements in the section of this chapter devoted to postoperative complications. For example, in speaking of the treatment of paralytic ileus, the authors state that "purgatives, colonic irrigation by high enemata, and use of certain drugs such as acetylcholine and prostigmine are the methods of choice." In cases associated with toxemia, they advocate the use of B. welchii serum in a massive subcutaneous dose of 60 to 100 c.c.

Breast Cancer and Its Diagnosis and Treatment. Edited by Edward F. Lewison. 477 pages with 181 illustrations. Baltimore, 1955, Williams & Wilkins Company. \$15.00.

The feeble grasp which we have of the problem of cancer is well illustrated by the status of breast cancer and its treatment. We know little of its cause and are divided as to the significance of pre-existing benign breast disease. With respect to treatment, 60 years after Halsted reported the operation which for the first time materially affected the course of the disease, some argue that "results" are a function of the biologic properties of the individual tumor, and there is wide disagreement in practice as to what constitutes a Halsted radical mastectomy, and there is no agreement as to the importance of wide skin resection, thin skin flaps, skin grafting. At the same time that one group of surgeons is making a practice of adding to radical mastectomy the extended mediastinal and cervical dissections which Halsted and his students had also investigated, another school has abandoned radical mastectomy in favor of simple mastectomy and heavy axillary irradiation.

Dr. Lewison's book, written with eight contributors, provides a very satisfactory review of the problem, in all its aspects and from various points of view. Some of the sections, "Diagnosis," "Surgical Treatment," tend to be prosy, unnecessarily detailed, and pitched at too elementary a level. Most of the sections by contributing authors are excellent. The chapter by Handley on surgical anatomy of the breast is a beautiful example of clear surgical writing. There are excellent sections on the pathology of cancer of the breast by Robert C. Horn, Jr., and on the extended radical mastectomy, by Jerome A. Urban.

The book is extensively and handsomely illustrated, perhaps overillustrated (Figures 81 and 83 are identical). The historical approach is a valuable aspect of the treatment of the subject. The author and many of his contributors refrain from editorializing and special pleading. There are wide and repeated comparison and analysis of the results of various clinics, with thorough bibliography, and this is perhaps the most valuable feature of the book.

Enfermedades de la Mamma. By A. E. Nogues. 626 pages with 191 illustrations. Buenos Aires, 1955, Lopez and Etchegoyen.

This is a well-written book on the major diseases of the breast. All disease entities are discussed from the viewpoints of etiology, pathogenesis, clinical forms, macroscopic and

microscopic pathology, diagnosis, differential diagnosis, prognosis, and treatment. To the end of each chapter is appended a concise review of the chapter. The bibliography is drawn from both English and European sources as well as Spanish ones, and great emphasis is placed on the American sources, especially in reference to carcinoma of the breast. An entire chapter is devoted to chronic cystic mastopathy, including a section on the relationship of this disease to carcinoma of the breast. There is also a single chapter devoted to the treatment of carcinoma. The relationship of carcinoma to pregnancy and lactation is also discussed.

The author has an open mind on many controversial subjects and freely points out the feelings and statistics of other authors on different subjects. Although all of the photographs are in black and white, those of the gross lesions are excellent. The Spanish in the book is easy to read.

Textbook of Endocrinology. Edited by Robert H. Williams. Second edition. 776 pages with 172 illustrations. Philadelphia, 1955, W. B. Saunders Company. \$13.00.

The increasing number of publications concerning endocrinology attests to the great interest this branch of medicine has provoked. The book under discussion is divided into thirteen parts, and there are ten different authors. These authors are outstanding authorities in their respective fields and have brought their subjects up to date. As a result several of the chapters have been completely rewritten since the first edition and the remaining chapters revised and amended.

As in the entire field of endocrinology so in this textbook, there are areas where one could disagree but on the whole the writers have presented the material and evidence for their opinions in an unbiased manner.

It is impossible to select any single chapter as outstanding. With the increasing interest attached to the adrenal cortex, however, it is refreshing to find this phase of the book handled so well.

The chapter dealing with laboratory procedures should prove of great interest to the neophyte in this field and particularly to the student.

The entire book is very readable and written in a manner that is conducive to a proper understanding of the subject. One important aspect of this type of book is the bibliography and it is most complete. Thus anyone desiring further information will have no difficulty in finding plenty of references.

Obstetrics. By J. P. Greenhill. Eleventh edition. 1088 pages with 1170 illustrations. Philadelphia, 1955, W. B. Saunders Company. \$14.00.

The appearance of a new edition of one of our standard textbooks is always a welcome event. The present volume has been so greatly changed that it bears little resemblance to DeLee's *Principles and Practice of Obstetrics* which first was published in 1913. Greenhill collaborated with DeLee, beginning with the eighth edition published in 1943. Just why the present volume should be called the eleventh edition is somewhat of a bibliographic puzzle since DeLee's name no longer appears on the title page and he is not mentioned in the preface.

The entire book has been rewritten. Numerous illustrations used in previous editions have been removed and 125 new illustrations have been added; 144 illustrations are in color. The author has enlisted the aid of fourteen specialists, a wise course in view of the fact that our knowledge of the specialty has grown so complex. Entirely new chapters have been added on roentgenology in obstetrics, analgesia and anesthesia, fetal crythroblastosis and the Rh factor, diseases of the nervous system, induction of labor, and prolonged labor. There is a special chapter on endocrine changes and diseases during pregnancy.

The first three sections of the book are devoted to the physiology and conduct of pregnancy, labor, and the puerperium. The chapter on analgesia and anesthesia is excellent.

A chapter on the psychology of pregnancy, labor, and the puerperium is largely the work of Helene Deutsch. Obstetricians today are aware of the importance of the psychological aspects of obstetrics, but at least some readers will be surprised to learn that in our time the "normal" mature woman is almost an illusion. Deutsch approaches the subject from the psychoanalytic point of view. She seems to be unduly pessimistic about the present conduct of labor by men. Many obstetricians will be amazed at the fear, the horror, the fury, and the frenzy Deutsch finds accompanying childbirth. Considerable emphasis is placed on the methods of G. D. Read and his followers.

Part II on the pathology of pregnancy, labor, and the puerperium, covers the abnormalities in a thorough manner.

The final section on operative obstetrics is excellent, especially the chapters on general considerations of operative obstetrics, preparatory manipulations on the baby, and breech extractions.

The special axis-traction handle of the Barton forceps, although mentioned, is neither illustrated nor its use described. The handle is an essential part of the instrument since most of the operation should be done with the handle. Many of us feel that axis traction is of value in all but the simplest low forceps, an enthusiasm which Greenhill states he does not share

An adequate number of references are placed at the end of each chapter and there is a fine index.

Greenhill's approach to the practical problems of obstetrics is a conservative one.

Annotated Bibliography of Vitamin E, Vol. III, 1952-1954. Compiled by P. L. Harris and W. Kujawski. 182 pages. Rochester, New York, 1955, Eastman Kodak Co.

This is a bibliography comprising 996 titles of papers published in 1951 through 1954. Many of the papers are abstracted briefly. The titles are arranged by classes, as "Occurrence and Distribution," "Determination," "Chemistry," "Physiology and Pathology," "Pharmacology," "Nutrition and Metabolism," and "Medical and Therapeutic Use." These classes are subdivided so that one may find together all papers relevant to a narrow interest. There is an authors' index of 13 pages.

This compilation should be of great value to the specialist, as a key to the literature. For the dilettante the abstracts offer a painless path to some knowledge of recent work in the field.

Correspondence

Ruptured Intracranial Aneurysm in Pregnancy

To the Editors:

The article, "Ruptured Intracranial Aneurysm In Pregnancy," written by Drs. Robert L. Feldman, Sidney W. Gross, and Seymour Wimpfheimer, which appeared in the August, 1955, issue of the American Journal of Obstetrics and Gynecology, pages 289-295, erred in stating that "there have been only 5 reported cases of a ruptured aneurysm of the circle of Willis during pregnancy or the early puerperium proved by angiography or necropsy."

A similar case, proved by arteriograms and subsequently operated upon with excision of the aneurysm, was reported by me in the Medical Woman's Journal, volume 56, page 17, 1949. This article was abstracted by Dr. James P. Marr, American Journal of Obstetrics AND GYNECOLOGY 60: 234, 1950.

EUGENE T. RUSH STONE, M.D.

816 HIGH STREET POTTSTOWN, PENNSYLVANIA Ост. 26, 1955

Administration of Oxytocics

To the Editors:

I enjoyed reading the article on "Elective Induction of Labor Using Pituitrin" by Dr. Edwin L. Hukill which appeared in this Journal, volume 70, page 972, 1955. He presents a large, well-analyzed study, but there are two major points with which those who are interested in the proper and safe use of posterior pituitary extract must take issue.

1. Pitocin and not Pituitrin is the agent of choice. Pitocin offers a maximum oxytocic with a minimum pressor effect and avoids drug-induced hypertension. In our large series 2 to which Dr. Hukill refers, Pitocin was used exclusively.

2. The preferred route of administration is by intravenous drip. Given this way, Pitocin evokes a more physiological laborlike uterine response than when given intramuscularly. This was shown by Hellman, Harris, and Reynolds.3 The rationale for intravenous rather than intramuscular Pitocin is clearly presented by Reynolds4 in his recent monograph which is "must" reading for those using Pitocin.

Indeed, Reynolds4 lists four safety factors which permit the obstetrician to avail himself of "safe Pitocin." Two of these are: (1) the use of Pitocin rather than Pituitrin, and (2) the use of intravenous rather than intramuscular administration.

As a result of the contributions made by Theobald, Page, 7, Hellman, and others, intravenous Pitocin has assumed its rightful place in our obstetrical armamentarium. I feel confident Dr. Hukill will agree that we must emphasize the proper and safe use of so valuable an agent lest it again fall into disrepute. I am sure he will accept these comments in this spirit.

MARTIN L. STONE, M.D.

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 Hellman, L. M.: Am. J. Obst. & Gynec. 57: 364, 1949.

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Nov. 8, 1955

Reply to Dr. Hukill

To the Editors:

Two important points have been rightfully emphasized by Dr. Stone. There is good evidence in the literature that Pitocin is preferable to Pituitrin and that the intravenous route is preferable to the intramuscular. Although my survey did not attempt to demonstrate any tendency of Pituitrin to elevate blood pressure or cause a reversal of uterine gradient, I feel its continued use represents a lag in adopting newer and better methods.

The administration of oxytocics intramuscularly by nurses under rigorous rules of supervision is shown to be a safe and practical system of inducing labor in large numbers of patients. Intravenous administration by the usual standards requires the constant attendance of a physician. This may not always be practical or possible where one must attend to other patients. Whether this fact or the less physiological action of the intramuscular route is more important may be problematical.

Dr. Stone's points of emphasis are undoubtedly even more important in the treatment of pathological states of labor. In almost all of our inductions, the oxytocic serves as an initial stimulus, spontaneous contractions taking over subsequently, and normal physiological patterns resulting.

In view of tremendous numbers of elective inductions now being done throughout this country on the basis of their harmlessness to the mother, wholehearted acclaim for any method should perhaps be made with reservations until better comparative studies are published on the effect of chemically induced uterine contractions on the fetus and the long-term results to the infant. As regards neonatal mortality, Dr. Stone's recent report on 1,222 inductions is very reassuring.

EDWIN L. HUKILL, M.D.

Reference

1. Stone, M. L., Gordon, M. S., and Folsome, C. E.: AM. J. OBST. & GYNEC. 69: 140, 1955.

100 THIRD STREET WATSONVILLE, CALIF. DEC. 21, 1955

Recommended Procedure in Prolapse of the Umbilical Cord

To the Editors:

Prolapse of the umbilical cord is an entity in which present-day therapy can hardly be regarded as completely satisfying. While the current trend is toward the use of cesarean section, one feels that surgery is not the ultimate answer.

The following unusual case holds out the possibility of a different mode of treatment. It is but a single observation, but it may be fruitful nevertheless.

Case History.—Mrs. M. B., Negro, aged 28 years, para iv, gravida v, date of last menstrual period unknown, entered the Dosher Memorial Hospital at 3:30 p.m. on May 31, 1954, after having traveled forty miles, partly on dirt roads. She had been in labor 10 hours and had started her journey to the hospital 1½ hours previously when her midwife had noticed the umbilical cord hanging outside the vagina. On admission, the patient was immediately placed in the Trendelenburg position. The bladder was just below the umbilicus and a diagnosis of twin pregnancy was made. It was noted that the cord was pulsating vigorously.

Ether inhalation anesthesia was begun and the bladder catheterized. As soon as the bladder was emptied, the cord stopped pulsating.

The cervix was fully dilated, and the first baby presented as a frank breech 2 inches above the ischial spines. It was converted to a footling and easily extracted at 3:57 p.m., almost 2 hours after the prolapse of the cord was first seen. The baby was a healthy 8 pound, 3 ounce boy who breathed spontaneously 3 minutes after delivery. Podalic version and extraction of the second baby, who weighed 7 pounds, 12 ounces, was performed 17 minutes later. The second baby was also healthy and commenced breathing spontaneously.

The possibility that the bladder acted as a cushion between the fetal buttocks and the pubic symphysis is indicated by the observation that the cord stopped pulsating imme-

diately after catheterization of the bladder. It appears that artificial filling of the bladder during the first stage of labor until the cervix is fully dilated may prevent compression of the cord. Thus fetal respiration may proceed unhindered until the cervix is fully dilated. Provided disproportion is not present, forceps or breech extraction may then be used to deliver the baby rapidly after the bladder is emptied. The period of anoxia will thus be a matter of minutes. While this procedure is still of unproved value, it can be rapidly performed without loss of time and an immediate assessment made of its efficacy.

NORMAN M. HORNSTEIN, M.D.

Southport, North Carolina Nov. 18, 1955

Item

"The Foundation Prize" of the American Association of Obstetricians and Gynecologists

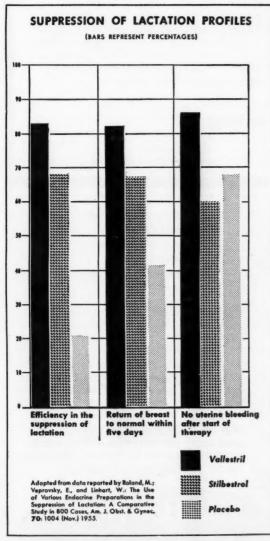
The rules governing the award are as follows:

- 1. The award which shall be known as "The Foundation Prize" shall consist of \$500.00.
- 2. Eligible contestants shall include only (a) interns, residents, or graduate students in obstetrics and gynecology, and (b) persons with an M.D. degree, or a scientific degree approved by the Prize Award Committee, who are actively practicing or teaching obstetrics, gynecology, or engaged in research in these fields. No fellow of the Association shall be eligible to compete for this Prize, and no candidate securing the award shall be eligible to compete again.
- 3. Manuscripts must be presented under a nom de plume, which shall in no way indicate the author's identity, to the President of the Foundation together with a sealed envelope bearing the nom de plume and containing a card showing the name and address of the contestant.
- 4. Manuscripts must be limited to 5,000 words, and must be typewritten in double spacing on one side of the sheet. Ample margins should be provided. Illustrations should be limited to such as are required for a clear exposition of the thesis.
- 5. The successful thesis shall become the property of the Association, but this provision shall in no way interfere with publication of the communication in the official Journal of the Association or, failing that, in a journal of the author's choice. Unsuccessful contributions will be returned promptly to their authors.
- 6. Three copies of all manuscripts and illustrations entered in a given year must be in the hands of the President of the Foundation before April 1st.
- 7. The award will be made at the Annual Meeting of the Association, at which time the successful contestant must appear in person to present his contribution as a part of the regular scientific program, in conformity with the rules of the Association. The successful contestant must meet all expenses incident to this presentation.
- 8. The President of the American Association of Obstetricians and Gynecologists Foundation, Inc., shall annually appoint a Committee on Award, which, under its own regulations, shall determine the successful contestant and shall inform the Secretary of his name and address by May 15th.

Inquiries for further details should be addressed to Frank R. Lock, M.D., Secretary, Bowman Gray School of Medicine, Winston-Salem, N. C.

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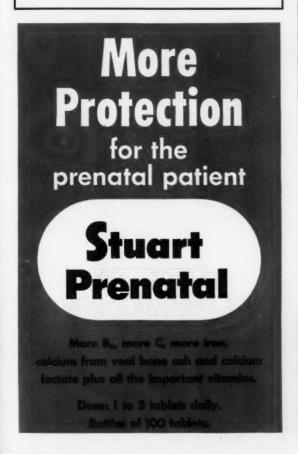
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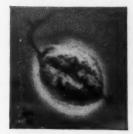
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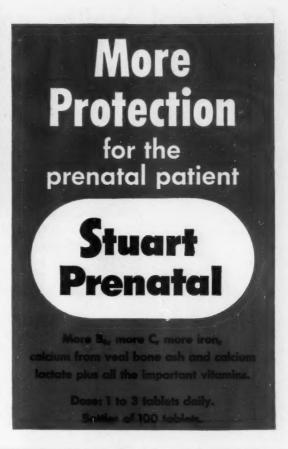
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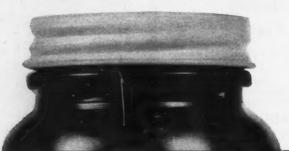
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VITAMIN	Dz, Cr	ysta	Hine	9			4	400	U.S.P.	Units
THIAMINE	HCI			٠					3.00	mg.
RIBOFLAV	IN								2.00	mg
NIACINAN	MIDE								10.00	mg
ASCORBIG	ACID			0					30.00	mg
CALCIUM	PANTO	THE	NAT	E					2.50	mg
PYRIDOXI	NE HO	1 .			0				1.00	mg
FOLIC AC	ID .								.33	mg
VITAMIN	B12 C0	nc.,	act	ivit	у е	qu	iv.	to	1.00	mcg
FERROUS	GLUCG	DNAT	E	0					100.00	mg
TRACE EL	EMEN	TS*								

*As Added Micronutrients

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